

THE AMERICAN JOURNAL OF PSYCHIATRY

Volume 148, Number 9 September 1991

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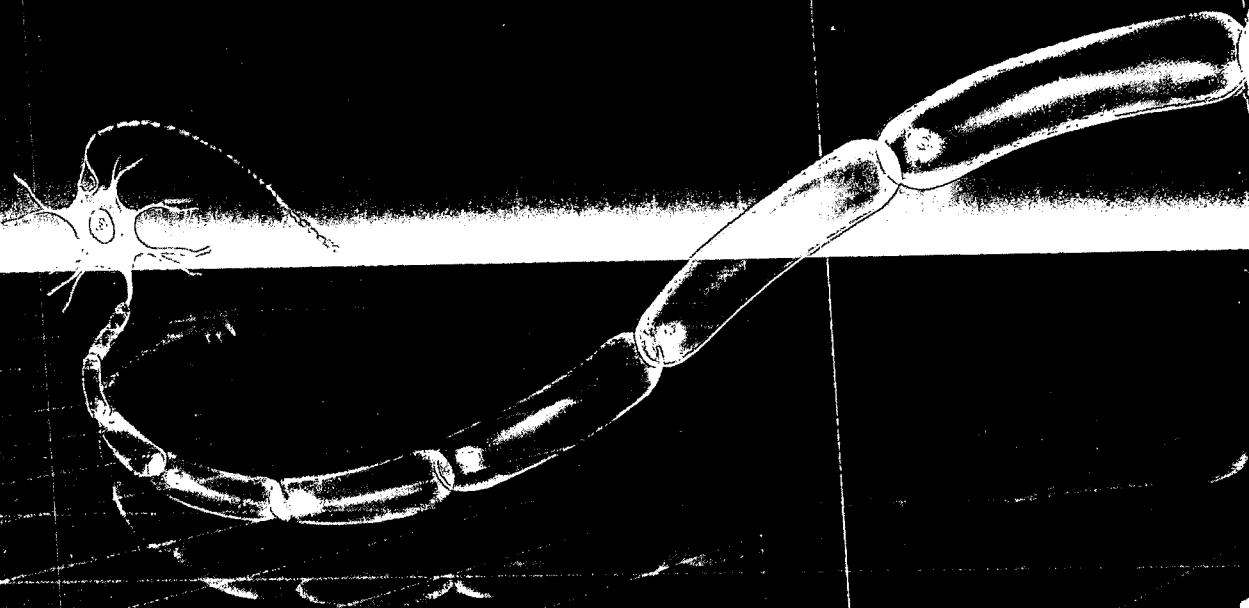
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Psychodynamics of Suicide,
With Particular Reference to the Young

By Herbert Hendin

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Type set by Byrd Data Imaging Group, Richmond, VA. Printed by The William Byrd Press, Inc., Richmond, VA. Printed on acid-free paper effective with Volume 140, Number 5, May 1983.

Second-class postage paid at Washington, DC, and additional mailing offices. POSTMASTER: Send address changes to *The American Journal of Psychiatry*, Circulation Department, American Psychiatric Association, 1400 K St., N.W., Washington, DC 20005.

Indexed in *Abstracts for Social Workers*, *Biological Abstracts*, *Chemical Abstracts*, *Chicago Psychoanalytic Literature Index*, *Cumulative Index to Nursing Literature*, *Excerpta Medica*, *Hospital Literature Index*, *Index Medicus*, *International Nursing Index*, *Nutrition Abstracts*, *Psychological Abstracts*, *Science Citation Index*, and *Social Sciences Index*.

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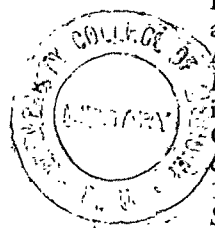
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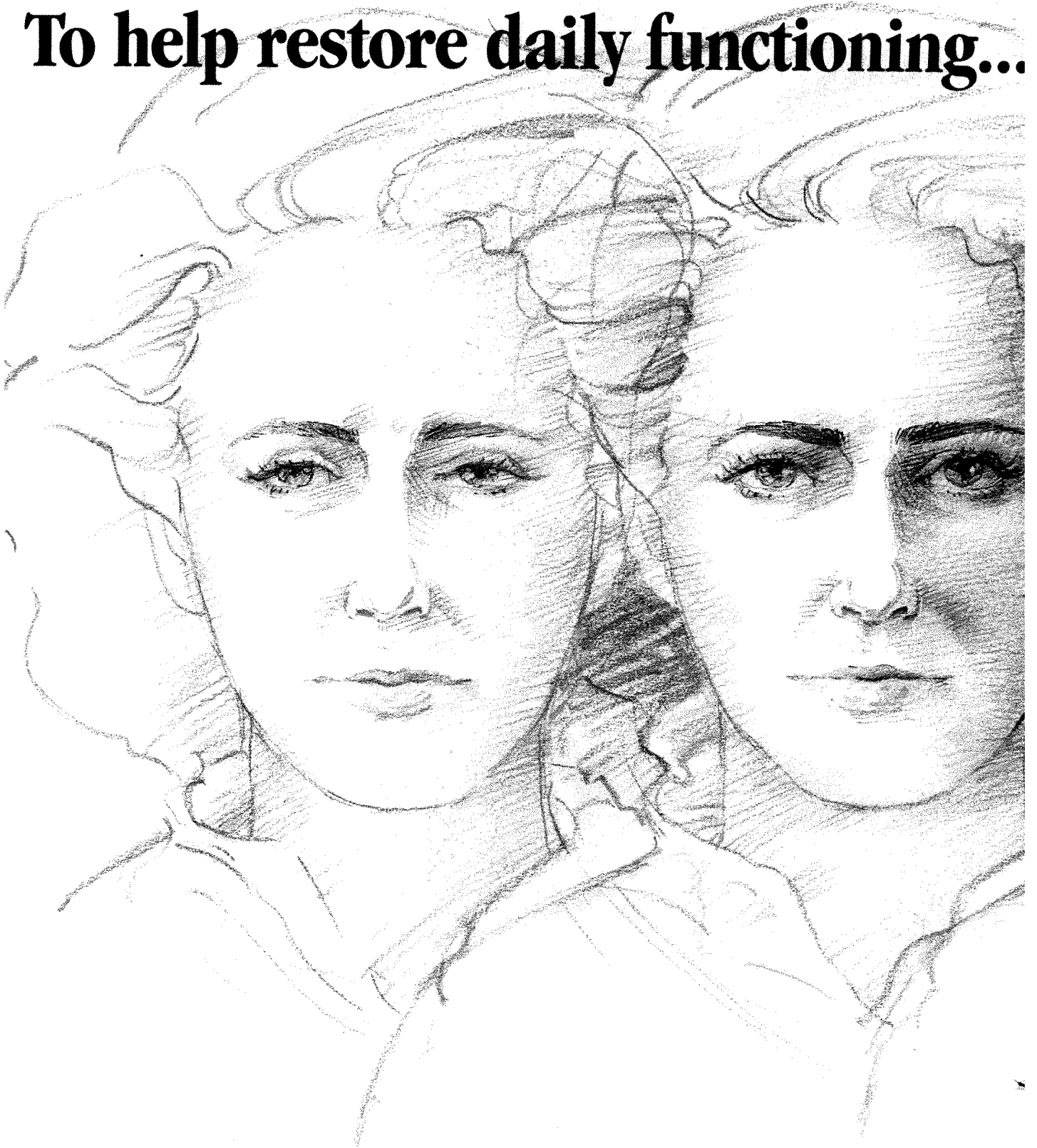
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The American Journal of Psychiatry, ISSN 0002-953X, is published monthly by the American Psychiatric Association, 1400 K Street, N.W., Washington, DC 20005. Subscriptions (per year): U.S. institutional \$85.00, individual \$56.00, student \$28.00; Canada and foreign institutional \$115.00, individual \$86.00, student \$43.00. Single issues: U.S. \$7.00, Canada and foreign \$10.00.

Business communications, address changes, and subscription questions from APA members should be directed to the Division of Member Services: (202) 682-6090. Communications from nonmember subscribers should be directed to the Circulation Department: (202) 682-6158. Authors who wish to contact the *Journal* editorial office should call (202) 682-6020 or FAX (202) 682-6016.

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Type set by Byrd Data Imaging Group, Richmond, VA. Printed by The William Byrd Press, Inc., Richmond, VA. Printed on acid-free paper effective with Volume 140, Number 5, May 1983.

Second-class postage paid at Washington, DC, and additional mailing offices. POSTMASTER: Send address changes to *The American Journal of Psychiatry*, Circulation Department, American Psychiatric Association, 1400 K St., N.W., Washington, DC 20005.

Indexed in *Abstracts for Social Workers*, *Biological Abstracts*, *Chemical Abstracts*, *Chicago Psychoanalytic Literature Index*, *Cumulative Index to Nursing Literature*, *Excerpta Medica*, *Hospital Literature Index*, *Index Medicus*, *International Nursing Index*, *Nutrition Abstracts*, *Psychological Abstracts*, *Science Citation Index*, and *Social Sciences Index*.

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Presidential Address: Looking Ahead: New Psychiatry, Old Values

Elissa P. Benedek, M.D.

Last year I prefaced my remarks by noting that it was a great personal and professional honor for me to address you surrounded by family, friends, and colleagues who had known and supported me from childhood, through adolescence, and into maturity with love, understanding, and encouragement (1). That sentiment is equally applicable today, and I should add that it is also a personal and professional honor to be surrounded by members of the family of APA who, similarly, have supported me through this challenging and inspiring year, which began in May 1990 in New York and which culminates this week in New Orleans.

The decision to hold another APA annual meeting in New Orleans has been a controversial one, of course, because the attempts by the state of Louisiana to restrict the availability of abortion is in direct opposition to APA's strongly held pro-choice policy. As the focus of this meeting, however, is on children and families and, perhaps implicitly, on the importance of every child being a wanted child, our presence in New Orleans should serve to support and encourage those from this state who endorse our policy and, we hope, make those who oppose it better understand the important basis of APA's long-standing position.

My year as your President has been a demanding but exciting one. I spent much of my time interacting with individual APA members, officers, and staff in order to both formulate and implement policies acted upon by the Board of Trustees and the Assembly. As a spokesperson for the Association, I also had the responsibility of articulating its positions to Congressional committees and their staffs, the media, the pharmaceutical in-

dustry, and to such entities allied with APA as medical groups, mental health organizations, and patient advocacy associations, as well as to the public. I was also able to bring back to our organization the concerns about psychiatry and psychiatric practice expressed by those to whom I spoke. Presenting organized psychiatry's position on critical issues is no trivial matter, and I did not hesitate to consult with the medical director, speaker of the Assembly, officers, trustees, relevant members of APA components, and the membership before doing so.

This was a year that saw the Association challenged on many fronts. Much of our attention was directed to important issues such as discriminatory insurance coverage, managed care, ethics, services for children and adults, research, legal matters, and the encroachment of other mental health practitioners into the practice of psychiatry, to name but a few. This was a year in which, although disheartened by the war, we did much, both as an Association and as individual members, to support our young men and women in the Gulf and their families, and we are thrilled by their triumph. It is hard to believe, though, that last year we were discussing the peace dividend and its implications for improving mental health services, and this year we are faced with unprecedented economic constraints on our Association and a need to assign priorities to our commitments and resources.

One of the more challenging tasks of the year for me was selecting a theme for the 1991 annual meeting and arriving upon some relevant remarks for this very special, if somewhat captive, audience. As I did before preparing for last year's opening session, I read the Presidential addresses and responses of my predecessors and noted, once again, certain recurring themes—respect for research; concern about changing economics; concern for the care of patients with compassion, humanity, and ethical integrity; and a need for creativity and personal dedication in challenging times. That these themes persist is neither coincidental nor irrelevant; it is inevitable.

Presented at the 144th annual meeting of the American Psychiatric Association, New Orleans, May 11–16, 1991. Dr. Benedek, 119th President of the American Psychiatric Association, is Director of Research and Training, Center for Forensic Psychiatry, and Clinical Professor of Psychiatry, University of Michigan Medical Center, Ann Arbor. Address reprint requests to Dr. Benedek, Center for Forensic Psychiatry, 3501 Willis Rd., Ypsilanti, MI 48197.

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The fundamental objectives, needs, and concerns of psychiatry (indeed, of all medicine), like the great questions confounding the philosophers, are never entirely put to rest and must be dealt with by each generation in its own time. I, too, will touch on these matters today, particularly as they apply to the theme I have chosen, "Our Children—Our Future." Incidentally, I am gratified that so many of you have indicated to me your enthusiasm for this theme, and, like you, I am looking forward to the various annual meeting sessions this year that will be devoted to children as well as to other areas of concern to our Association, and I am delighted to see all of you here.

As I have stated, the universal issues remain, always to be considered against a backdrop of change. During the past 30 years, psychiatry has experienced changes of great magnitude. The theoretical basis of psychiatry, for example, has shifted from a largely psychoanalytic to a biopsychosocial approach, and successful new treatments and psychopharmacological agents are available. Hospitalizations are now brief, if not dispensed with entirely. Patients return to the community with a degree of dispatch unheard of in the past, sometimes too soon. Not only are patients' families participating in the therapeutic process with greater frequency, but their involvement is becoming more extensive. As suggested, not all changes have been positive. For instance, many of us have grown more and more concerned as third-party payers encroach upon medical decision making, and in response to these concerns APA has been taking action that I will discuss a bit later. It seems inevitable that further changes of comparable magnitude will occur during the coming years, with implications that we cannot foresee other than the certainty of still greater challenges to our profession.

Last year I told you the story of "Missy," a 10-year-old who endured parental mental illness and violence, a youngster who grew up in a cycle of abuse and neglect. I shared with you my concerns about helping her. I am happy to report progress in her treatment, and although the therapeutic gains are still limited, from the perspective of Missy's life, they are important and consequential. This year I would like to tell you about another child, a child I saw 30 years ago when I first began to practice psychiatry as a resident.

Unlike Missy, "Susan" was a child of middle-class parents, raised in a small upper peninsula Michigan town. Her parents brought her to a university hospital for treatment because of their concern about her persistent and unusual habits. Before going to bed each night, Susan would meticulously line up her shoes, teddy bears, dolls, and other toys with almost military precision. The lines never deviated from night to night. Susan washed her hands some 10 or 12 times a day; often they were raw and bleeding. Although Susan was a bright, perhaps even gifted, child, her progress in school was minimal because of her need to dot and redot her *i*'s, cross and recross her *t*'s, and check and recheck that every word on the page was properly, in fact, meticulously, aligned. Because of her time-con-

suming thoughts and habits, Susan was isolated and withdrawn from her family and peers.

Susan was admitted into one of the best children's hospitals in the country because she was considered "a good training case." I was asked to be her treating physician. She was placed on an inpatient psychiatric ward with autistic, psychotic, and delinquent children and adolescents. The principles of treatment, in a word, were as rigid and compulsive as Susan. For example, Susan underwent play therapy 2 hours every week; neither she nor I was allowed any contact with her parents; and no medication was used. Although Susan's mother and father were blamed for her illness, there was no family therapy, and they were seen only intermittently by an allied mental health professional. Needless to say, there were no support groups or organizations for them to join.

Susan's parents paid out of pocket for their daughter's 2 years of psychiatric hospitalization. At the time of her discharge, it was clear that she had vastly improved. Her strange habits had disappeared, and she appeared cheerful and was no longer withdrawn in the company of the other child patients. But when she returned to her home and community, she was immediately extruded. Her parents had rented her room to a boarder, and her community of other children teased her because she was a stranger who had been in a psychiatric hospital. They called her "crazy" and "loony."

Susan and her family did not return for outpatient therapy or outreach—which was not even an entry in the psychiatric lexicon at that time. I only learned the sad facts of her return home when Susan came to see me last year, 30 years after her discharge. She was now a graduate student at the same midwestern university where, as a child, she had been hospitalized, and, once again, her obsessive concerns and compulsive habits had surfaced and interfered with her ability to do graduate-level work. She was in therapy with another psychiatrist. One of the overwhelming concerns she shared with that psychiatrist was her "craziness" as a child. Why had she needed to be hospitalized for 2 years? What had she done to compel such a lengthy hospitalization? Why had she been on a unit with children she remembered as bizarre and out of contact with reality? What had been done for or to her by her parents, fellow patients, and her therapist? What illness might she transmit to her young children?

Susan's therapist ingeniously recommended that she visit me, which she did, and together we reviewed her past records and the treatment available to mentally ill and emotionally disturbed youngsters in the 1960s. We confronted many of the biological, psychosocial, legal, and ethical issues that her situation had presented at the time and how these would have been dealt with in 1990. We talked extensively about how treatment advances in the ensuing 30 years would have made her long hospitalization unnecessary and undesirable. We also discussed how differently her relationship with her family and her family's relationship to treatment would have been viewed today. Susan's therapist later called

to share with me the extraordinarily beneficial effect that this consultation had had on Susan.

I have chosen to share Susan's story with you for three reasons. First, because this has enabled us to reflect upon the path that child psychiatry has traveled during my 30 years of practice and, thereby, to demonstrate how this revolution in psychiatric treatment has enhanced the quality of clinical care that we are able to provide. Second, so that we can use the changes of the past 30 years as a springboard for examining the problems that have persisted or emerged. Finally, because Susan's case reminds us of the inevitability of change and the need, therefore, to both think about—indeed, to influence—the future and continuously reexamine our traditional values and humane standards in the provision of clinical care. So, having considered the changes that have occurred during the past three decades, let us turn to some of the problems that we are now facing.

Despite the fact that for at least 20 years there has been widespread agreement in the mental health community on the need for a coordinated and flexible system of care for children with mental health problems, public policy in this area remains underdeveloped. Given the number of children so afflicted, this state of affairs is nothing less than shocking. Approximately six to eight million youth have serious mental health problems. Yet less than half of them get any form of treatment, and those who do often receive inappropriate services. We have discovered this, ironically, at a time when two decades of advances in child and adolescent mental health research hold out promise of help and recovery to so many more. Consider, for example, the wealth of different child therapies that have become available since Susan's hospitalization. They are based on theoretical perspectives as diverse as child psychoanalysis, behavioral therapy, family therapy, and systems therapy. Although play therapy and individually oriented psychodynamic therapy are still important, other frequently used therapies for children include group therapy, behavioral therapy, family therapy, pharmacotherapy, milieu therapy, and crisis intervention. The treatment armamentarium has been expanded and diversified as more specific treatments are being adapted to specific disorders and specific environmental traumas.

Children's mental health services, although still offered primarily within the hospital, are now available in a variety of settings, and the choice of setting, naturally, will have a great bearing on both the therapeutic effect and the cost of treatment. Perhaps one of the most important trends has been the increasing privatization of care, particularly inpatient care, and the general increase, therefore, in the use of private psychiatric hospitalization. Decreases in the number of children treated in state and county hospitals have been offset to some extent by substantial increases in the use of private hospitals.

There continues, however, to be a dearth of community services. As in Susan's situation, treatment resources

are still essentially focused upon the relatively small number of children who need inpatient facilities or other residential treatment. This invites overuse of private psychiatric facilities because funding, although inadequate and diminishing, is still available for hospital care, and public institutions are being closed.

In its 1990 report, "Care of the Seriously Mentally Ill" (2), the National Alliance for the Mentally Ill recognized that the public mental health system, including care for children, is a disaster. Psychiatrists unjustly have been blamed for its failure. The public system has not been reexamined, modernized, or adequately funded, and, if anything, this penalizes those dedicated psychiatrists who continue to work within its structure. The lack of community-based services has allowed many, children in particular, to fall through the system's steadily widening cracks. Be assured, there would be no calamities such as this if more people listened to us.

The problem of scarcity of services is compounded by the absence of coordination of those limited services which are available. They are often fragmented among traditional health service agencies, departments of special education, rehabilitation services, mental retardation services, departments of developmental disability, and the juvenile justice system. Such fragmentation causes difficulty for psychiatrists because it requires us to function outside the traditional medical environment. Thus, two important factors that continue to limit the prospects of appropriate care for children are the structure of health care financing, which rewards inpatient hospitalization, and the lack of coordination, and often cooperation as well, among agencies that provide services for children.

As suggested, one reason that hospitalization, particularly in private facilities, is extensively relied upon is because private health insurance generally pays for hospitalization but rarely offers reimbursement for alternative programs. Even with such hospitalization, however, private health insurance benefit packages usually make no distinction between children and adults. Children, therefore, are subject to all the well-documented limitations in funding. While limited benefits are a concern for all of our patients, financial and social costs associated with mental disorders in children and adolescents present special consideration. These include unusual diagnostic characteristics, duration of illness, and developmental problems. For example, we are now confronted with the long-term psychiatric implications of such clinical conditions as fetal alcohol syndrome; AIDS; problems resulting from mothers' use of "crack"; developmental disorders such as autism and retardation, which begin in childhood and last through life; and schizophrenia, which becomes manifest in the late teen years to early 20s and also lasts through life.

Although this would be bad enough, one should not infer from the foregoing that current problems are limited to providing adequate care for children. Nothing could be further from the truth. Our understanding of the brain and mind and their interaction with the body is growing so rapidly that it is difficult for us to remain

current. This has led to pressures for subspecialization and recertification. Geriatric psychiatry and substance abuse have recently been approved for added qualifications as subspecialties, and forensic psychiatry is close to obtaining approval as a subspecialty. Thus far, we have dealt with the problems inherent in the development of subspecialization without fragmentation of our organization, and we must continue to do so.

The changing economic environment, similarly, creates an unprecedented set of problems and constraints. In fact, many feel that they put the very future of psychiatry in doubt. I do not for a moment share this pessimistic view. The rate of change in the economic aspects of medical care, however, has been exponential. It is now rare for families to pay psychiatric costs directly. In the past 30 years, we have seen many innovations in the financing of health care, such as the introduction of Medicaid and Medicare, the rapid growth of prepaid, capitation care plans, the cost-conscious purchasing of health insurance by employers, more aggressive utilization management, and the recent introduction of relative value scales.

But these innovations have not resulted in access to psychiatric care for the entire population. On the contrary, the poor, the uninsured, the unemployed, and the marginally employed have been locked out of the mental health system. As noted, they cannot turn to their traditional ally, public psychiatry, with state psychiatric hospitals, large city hospitals, and large teaching hospitals closing units or closing their doors because reimbursement does not cover the cost of providing care or teaching. The problem of providing psychiatric care for the mentally ill homeless is even more troublesome. Since they almost never have any contact with the traditional health care system, there is a critical need for creative, mobile outreach services to provide food, clothing, and medical and psychiatric care. It is not surprising that the Institute of Medicine's Committee on Health Care for the Homeless concluded that the first priority in addressing problems of the mentally ill homeless is to ensure adequate availability of clinical services and supervise supportive housing arrangements.

We should not be deceived into believing that current public policy designed to contain health care costs has left unscathed children and adults who do have insurance. Indeed, both psychiatrists and mental patients, historically, have been victims of stigma and misunderstanding and have been particularly affected by cost-containment efforts. The fact is that since the inception of third-party coverage, psychiatry has never achieved parity with other medical services, and the emphasis on cost containment and managed care has caused further deterioration of an already bad situation. In 1983, merely 8 years ago, only 53% of employed workers surveyed by the Bureau of Labor Statistics had coverage for inpatient treatment of mental illness that was equal to their coverage for other illnesses. In 1986 the percentage of employed workers who had equal coverage for inpatient mental illness had fallen to 37%, a 16%

drop in just 3 years. By like token, coverage for outpatient treatment reflected inadequate limits, unrealistic constraints on the number of compensable visits, significantly increased copayment levels, and a number of other deterrents to adequate care. Of course, restrictions such as these reduce access to care and compromise both its quality and continuity.

Since 1986 we have seen the introduction of a new limitation—the advent of managed care. We must bear in mind that “managed care” is, more or less, a generic term, and therefore, so-called managed care programs can be very different from one another. For instance, some deal only with such requirements as hospital pre-certification and concurrent review, while others encompass organized service systems that clearly identify access and providers and offer the full spectrum of care. As insurers, employers, and others who pay for health care seek to curb its costs, one conclusion seems inescapable: for better or for worse, managed care in some form, at least for the foreseeable future, is probably here to stay. Thus far, this has been perceived, quite justifiably, as essentially a setback for psychiatry. For example, our judgment as psychiatrists has been questioned by reviewers who not only possess less education and training than we do, but also have no long-term commitment or responsibility to patients. We are frustrated and angered when we see termination of benefits for patients who are in dire need of psychiatric services. For families with young children, who are typically attracted to health maintenance organizations or other managed care plans, these plans may be particularly problematic, especially if a child has a chronic illness, since the lifetime maximum benefit level is reached in short order, leaving the child uninsured in the future. We are distressed that insurers seem unwilling or unable to recognize that appropriate, prompt, high-quality treatment of mental disorders leads to increased employee productivity, decreased absenteeism and employee turnover, and less comorbidity. Certainly our ability to make any impact on managed care systems has been agonizingly slow.

I would like to direct the balance of my remarks to a few thoughts about the future. As I noted earlier, and as Susan's case so graphically illustrates, change—rapid change—is inevitable. I am convinced that we can influence that change, but, while doing so, we must be ever mindful of the need to maintain traditional values and humane standards in the provision of clinical care.

I have already described the discriminatory economic policies that unfairly penalize persons with psychiatric disorders and the absence of high-quality mental health care for the poor and underinsured. Suffice it to say that these conditions are not only unacceptable, they are abhorrent, and we should and can and will keep hammering until they are eliminated.

With respect to managed care, a significant piece of the puzzle, I have discussed those consequences of its implementation that have given rise to almost universal consternation. We cannot and will not tolerate those consequences.

On a more encouraging note, managed care—responsible managed care—holds out the possibility of a full spectrum of care being developed for many patients. Indeed, some responsible managed care firms already profess commitment to the idea of instituting flexible benefits, including outpatient care, day care, evening hospitalization, residential care, and group therapy sessions, which may be substituted for the traditional inpatient hospital benefit. Responsible managed care companies could enable patients to obtain the necessary level of care and help avoid costly, and even unnecessary, hospitalization.

During this past year, together with other APA officials, I have met with responsible leaders in the managed care industry and shared our concerns, frustration, and anger. We underscored what we believe to be the most serious consequences of cost containment, specifically, undertreatment and premature discharge of patients from treatment and the failure to use treatment modalities that are in the best interests of a patient because the industry considers these too specialized or costly. The managed care people shared their perspectives on psychiatric care and, among other things, urged the rapid development of practice guidelines by the profession.

Such meetings are just one strategy that we in the Association have developed for dealing with the problems that have been caused by managed care. Other strategies include preparation of a managed care survival manual, drafting model legislation to regulate utilization review, and research and data collection. We are also considering litigation. Between May and October 1990, the APA managed care hotline detected 121 cases of "interference with professional autonomy and difficulty in providing quality patient care." This past year, APA joined with the rest of medicine and with consumer groups, such as the National Alliance for the Mentally Ill and the National Mental Health Association, to further explore ways to cope with this incursion and interference in the doctor-patient relationship.

If the managed care industry as a whole continues to be unresponsive to our concerns and does not offer benefits or alternative treatment settings, such as partial hospitalization and residential treatment centers for adolescents and children, the gains that our profession has made over the past 30 years in prescribing flexible and appropriate treatment and continuity of care will be lost. We simply cannot put up with this. Managed care and de facto rationing must not be allowed to compromise quality of care.

Maintaining appropriate areas of responsibility among mental health professionals is another challenge now facing our profession. This, of course, is fundamental to the provision of high-quality mental health care. When I treated Susan 30 years ago, there were discrete boundaries separating the roles and responsibilities of psychiatrists, psychologists, and social workers. Psychiatrists diagnosed and treated children, psychologists conducted psychological testing, and social workers worked with patients' families. By now, those

boundaries have become blurred because we recognize that there are overlapping areas of expertise. Certainly, allied mental health practitioners make important contributions to patient care. We also recognize, however, that medical training and the physician identity of psychiatrists ensure essential aspects of basic patient care, particularly in light of the existence of comorbidity in psychiatric patients and the understanding that mind and brain do not exist independently of the body. Recent proposals to permit psychologists in the military to prescribe psychotropic drugs after a brief and inadequate period of training represent a singularly inappropriate and offensive blurring of boundaries and a heedless sacrifice of quality care. If implemented, these proposals will not make psychiatric care more available to the chronically mentally ill, the poor, the underinsured, rural populations, or even to military personnel and their families. They will not reduce costs or lead to better psychiatric care. On the contrary, they will be regressive and destructive, and we will, most assuredly, continue to oppose them.

Another challenge to our profession in the 1990s is to secure increased research funding so that we can build on the enormous gains that we have made in expanding the scientific base of psychiatry, a base that continues to influence the understanding, diagnosis, and treatment of mental disorders. Discoveries in the past 10 years that have had an impact on the clinical practice of psychiatry include the rapid expansion of knowledge in the neurosciences and the expansion of technological innovations in clinical practice. Because of research, we have new and effective models of short-term psychotherapy, new and effective medications, and new and effective diagnostic procedures. And we have learned to enhance the effectiveness of treatment by combining medications, psychotherapy, and behavioral treatments as well as by including families and communities in our treatment planning. Thus, it is important that we continue to push for increased research funding, and I feel certain that we will.

As we progress further into the 1990s, however, we must continue to balance effective use of advances in brain science and technology with an increased understanding of and continued research on psychosocial influences on behavior, the psychosocial aspects of new technologies, and systems of care, as all of these will influence contemporary practice and ethical values. Since we, as psychiatrists, recognize that a patient is not a disturbed brain, an imbalance of neurotransmitters, or a diseased heart but a human being who deserves dignity, respect, and ethical care, we must continue to lead the way for all medicine as we confront new ethical issues.

During the past 30 years, organized psychiatry and the consumer movement have become a social force that has influenced psychiatrists to examine their professional roles more diligently and to be among the first to include patients and families in decision making. Moreover, the abuse of psychiatry in other countries—for example, diagnosing political dissenters as mentally

ill, committing them to hospitals, and treating them coercively and inappropriately—has compelled organized psychiatry to attempt to end international abuse and also has resulted in a greater awareness of ethical issues internationally. Contributions of professional disciplines such as law, sociology, psychology, theology, philosophy, and other areas of medicine also have led psychiatrists into thinking about the ethical dimensions of their work.

Contemporary interest in ethics among psychiatrists should not imply that we need more guidance than other professionals; it does suggest, however, that, like all professionals, psychiatrists need ongoing interpretation and instruction in their code of ethics. A reasonable argument could be made that as members of society, psychiatrists can rely on ethical principles that have been identified and valued by society as a whole. Braceland in 1969 (3) advanced the notion that the doctor/psychiatrist as a citizen must be an ethical person and act in accordance with the accepted standards that apply to all humankind. Although true, this does not go nearly far enough. If we examine the kinds of problems that psychiatrists routinely face today, it becomes apparent that many aspects of our professional activity raise special ethical issues that force us to both scrutinize and reinterpret our canons of ethics. For example, psychiatrists are regularly confronted with the imposing task of evaluating the state of a person's mind to determine whether sufficient evidence of mental illness exists to deprive that person of liberty or absolve him or her of social responsibility. Furthermore, the intimacy of the therapeutic relationship itself creates special risks, and, unfortunately, the current economic climate may entice some into placing profit before their patients' well-being.

By like token, although our Association's resources may be scarce, we must resist any temptation to direct all of them exclusively toward meeting economic challenges. I believe that we have a responsibility to constantly review our ethical principles to determine when there is a need to reinterpret, modify, or add to them in light of contemporary social issues, such as AIDS, abortion, the danger of compromised confidentiality in the age of computers, and the rationing of health care. This applies both to those problems unique to psychiatry and to those endemic to all of medicine, especially under today's constraints of cost containment and resource rationing. We must participate in the establishment of ethical standards of practice, and we must also monitor our compliance and take appropriate action against those who do not adhere to the standards that have been set. We must do this not out of fear that otherwise some other agency will do it for us or even because, due to our thorough understanding of our profession, we are best suited to do so. Rather, we should see this as nothing more nor less than our obligation if we are worthy of being called professionals.

The next 10 years will bring the greatest changes that any of us in psychiatry—in all of medicine, for that matter—have ever seen. This portends a very difficult pe-

riod, but also one of extraordinary opportunity. As we move toward, and then into, a new millennium, what is it that we want to achieve? Toward what goals should we direct our time, energy, and resources? As we determine our policies and formulate our plans, there are a number of points that we should bear in mind. I will conclude my remarks by enumerating 10 of them.

1. To be most effective, our Association must continue to develop consensus positions that serve the entire profession as opposed to subspecialty or special interest groups. This means that we must remain flexible and amenable to negotiation and compromise.

2. The Association should also continue to maintain ties to and work with diverse groups, such as allied mental health professionals, government agencies, consumers, insurers, and employers, and when appropriate, we should continue to form coalitions that are in the best interests of our patients.

3. It is imperative that we retain the capacity to control the quality of care that we give to all our patients. Having this dictated by others less knowledgeable, caring, and committed than we are can never be tolerated.

4. We must persevere in our efforts to attract the highest-quality medical students to residencies in psychiatry and child psychiatry. Similarly, no young man or woman should be deterred from entering medical school by inadequate funding that makes inevitable excessive, long-term indebtedness after graduation.

5. The rapid growth and expansion of our science places new importance on the continuing education of our members, as well as on the need to reeducate those who have fallen behind.

6. It is essential that we maintain the highest standards of practice and have the capability to eliminate from our midst those who are unwilling or unable to meet our high moral and ethical standards. It is also essential that we have the correlative ability to rehabilitate those who have had difficulty but who possess the capacity and will to alter the patterns of their lives and practices.

7. We are entitled to, and should receive, adequate compensation, compensation that is commensurate with the education and training, skill, commitment, and responsibility that characterize members of our profession.

8. A healthy, clean environment for our patients and for ourselves is an essential ingredient of an acceptable quality of life and is relevant to good mental health. It behooves us to play an active role in its development.

9. We should continue to use the prestige and influence of our Association to promote social causes that have a significant impact on quality of patient care and the mental health of our patients, as well as that of our colleagues, our children, and ourselves.

10. We must always strive to advance the science of psychiatry, deliver more astute diagnoses, provide more effective treatments, and ultimately, prevent mental illness.

The year 2000 is near. When it arrives we do not want to be in the uncomfortable—indeed, intolerable—position of having to tell patients such as Susan that the

gains we achieved between 1960 and 1990 were allowed to slip away because of our country's obsession with the "bottom line" rather than a commitment to its unfortunate and suffering citizens. Instead, if we continue our hard work, as individuals and as an Association, I am absolutely convinced that we will be able to say that we succeeded not only in staving off the collapse of today's failing mental health system but in creating a viable, strong, flexible system whereby every American, of every age and background and regardless

of socioeconomic status, is able to receive the care that he or she needs and deserves.

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Response to the Presidential Address: Humane Values and Biopsychosocial Integration

Lawrence Hartmann, M.D.

It is an honor to be here, to be APA President-Elect, and to address you all. It is an honor to follow and to try to respond to Dr. Benedek, whom I have liked and admired and largely agreed with for many years. And it is a pleasure to be surrounded by family and friends and colleagues. Many of you have helped me, inspired me, given me pleasure, and taught me in countless ways for many years, and I am very grateful.

Like Dr. Benedek, I have read and learned from some of our predecessors' opening session speeches. I noted that the President-Elect is asked to be briefer than the President (I will try to do that) but also to *respond* to the President. In my study of past addresses, however, I found perhaps a subtle tendency toward—what shall I say?—a bit more vigorous autonomy and independence than clear-cut responsiveness. That left me an interesting choice. I did something potentially a bit simple-minded and intrusive: a couple of months ago, I asked Dr. Benedek to send me a draft of her Presidential address, so that I could respond. She did so, and I thank her, and will spend a few moments responding to it before adding some more autonomous words.

Her speech covered a lot of ground, beginning by reminding us that our meeting in New Orleans has been somewhat controversial because of a particularly extreme stance that the Louisiana legislature has taken against abortion and against the pro-choice policy that APA has long favored. We have work to do to educate the members of the Louisiana legislature and the minority of Americans who more or less agree with them.

Dr. Benedek also rightly notes recurrent Presidential themes of respect for research, economic problems and challenges, and concern for compassionate clinical and scientific care of patients. She notes sadly—and I share her dismay—that last year's hopeful idea of a post-cold war peace dividend for social and mental health needs has all but vanished; that reflects not just the Gulf war and the recession but also major governmental and societal choices.

She tells us about a patient seen 30 years ago and talks of rigidity and family exclusion and lack of outpa-

tient follow-up after a 2-year hospitalization. I was trained at about the same time, and I know that such things existed, but I also know that already in the 1960s there was, where I trained and have since worked, at least a good deal more common sense and family involvement (individual and group) and insistence on outpatient follow-up and even outreach than her patient then received—but also *more* than is *now* provided in my state (which, like many states, is currently rapidly withdrawing from mental health services). I mention this because I am far less clear than she that we have had a “revolution” in psychiatric treatment, as she recently put it, “generally to the patient's benefit.” I think that we have gained and we have lost.

Dr. Benedek is shocked, and so am I, that public policy is still so underdeveloped in an area in which for over 20 years the mental health community has agreed: the need for a coordinated spectrum of care for children with mental health problems. But one lesson from that is that often, to have the mental health community agree is not enough. We urgently need to develop more political and economic clout for our values.

Dr. Benedek does not disavow the word “disaster” applied to our public mental health system for children by the National Alliance for the Mentally Ill, and neither do I. There are, as she points out, far too few community resources; the structure of health care financing is inadequate, full of gaps, and skewed; and there is nearly ubiquitous lack of coordination. I may return to that later in this address.

After usefully calling our attention to the huge challenge of AIDS and of drugs such as alcohol and “crack,” Dr. Benedek ties this to the growth of subspecialization and notes how many people are largely or fully *left out* of the mental health system, including the poor, the unemployed, and the homeless. Homelessness and leaving people out—far worse here than in Western Europe—is a terrible black mark on America at the end of the twentieth century.

Dr. Benedek talks of stigma against mental illness and psychiatry, and the tradition of inferior insurance coverage; and she talks of *managed care*. Managed care, variously defined, is very much here and very popular with government and business; it is far less popular with psychiatry, since, despite some reasonable potential, in many of its forms managed care has had major intrusive, reductive, and destructive effects on good care of patients. (APA is currently trying to work on and help shape managed care on many fronts.)

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Then there are roles and boundaries among mental health professionals. They used to be clearer. Psychologists' demands for control of admissions and inpatient care, and now of prescribing, should probably be seen primarily not through reductionist economic lenses, as guild issues, but through professional and patient care lenses, as safety and *quality of care* issues.

Dr. Benedek also reminds us of the continuing need for research and research funding, for balance between brain science and psychosocial research, for ethics, and for responding to the challenges of the 1990s. Like her, I firmly favor our continuing to promote important social causes that greatly influence both psychiatric care and the mental health of our patients, ourselves, and our children.

I like Dr. Benedek's points and emphases. What follows will be a few additional thoughts.

APA Presidents-Elect are expected not only to be interested in everything but also to choose a theme. As you may know, I have chosen "Humane Values and Biopsychosocial Integration." Some of you have noticed that those words are one way of celebrating the *clinician* in psychiatry because they describe what good clinicians live by and do.

Humane values require us, in promoting mental health and fighting mental illness, to be aware of and care for and treat whole people in context and over time: whole biological-psychological-and-social people in context and over time. Humane values require doing, teaching, researching, preventing, and, realistically, getting involved in some political and economic and public affairs areas on behalf of mental health. Humane values should also lead us to special interest in the underdog and those who are different. In my case, this has involved international affairs and ethics and human rights, but in all our cases it should involve interest in the old and the young, in cross-cultural psychiatry, American Indian issues, black issues, Hispanic issues, Asian-American issues, gay issues, and women's issues. To be humane to ourselves, we all have to select some areas of *special* interest, but we can retain an active view of the whole field around our expertise.

None of us can know everything about psychiatry. It often gets harder as we learn more. It may even be harder than it used to be even to respect those who know and do different things. Currently lively fields such as brain imaging, molecular genetics, and psychopharmacology are hard to keep up with, but they also contain risks—for instance, risks that we become so fascinated by one part of the biopsychosocial whole that we ignore and forget other parts. Such fields require continual integration and cross-fertilization with traditional and still vital other areas of psychiatry, and that is often hard to do. Some of us, I think, are guilty of biological reductionism, just as some of us are, or recently were, guilty of environmental or psychodynamic reductionism.

All the psychiatric patients I have ever seen seem to me best looked at biopsychosocially, even if the likely strategies for understanding and helping one

may be more in one realm, for another more in another. All patients—an abused child, a drug-abusing teenager, a neurotic graduate student, a schizophrenic adult, a depressed elder—deserve integrated biopsychosocial understanding and help.

Let me give you a short clinical vignette—although clearly no single vignette will do. I offer it not as proof but as one illustration. A few days ago, a psychiatric resident I supervise presented the case of "Jason." Jason is 10 years old, a physically healthy if somewhat plump black boy, fairly bright, articulate, and volatile. Jason has no friends. He has been briefly hospitalized for wild behavior and disregard of limits, which wore out and frightened his special classroom teachers and his mother, and for suicidal ideas and threats that included some action with a knife. Jason's mother feels inadequate and has a history of chronic depression. Jason's father, strange and evasive and usually absent, has recently fully moved out; he turns out not just to have a second (common-law) wife and household, with children, but to prefer that household. Jason's one sibling, a 15-year-old sister, has for many years been angry, badly out of control, and considered hopeless by her parents; she recently bore a child, who now lives with her and Jason and Jason's mother. Jason has been called hyperactive and has had variable learning and attention difficulties. His talk and play in therapy are marked by neediness, insecurity, sadness, anger, and confusion.

I could spend far more time than we have discussing Jason's and his family's biopsychosocial diagnostic and therapeutic issues; but for present purposes, let him stand as an example: for Jason, as, sometimes more subtly, for all patients, biopsychosocial thinking is essential. Less won't do.

Varied psychiatrists, all of us, can continually learn from one another and think and act with biopsychosocial interactive complexity in mind. In all our roles, we can and do develop special expertise, but we can also be integrators, respectful of complexity and able to act with and within complexity, trying always to be both scientific and humane—rather than giving in to ads and fads, premature closures, financial pressures, or mindless or brainless reductionism.

Tolerating, working with, and mastering complexity can be one of psychiatry's great strengths. Clarify, yes. Simplify, not always.

I think major splits have developed in American psychiatry over the past 25 years, and not just as a reasonable or proportionate response to previous overenthusiasms or to good new knowledge in brain biology on the one hand, or social and environmental factors on the other. Subspecialization is here and has many advantages. But good subspecialization must retain awareness of the whole field.

Moreover, splits come in various shapes. There is an old tension between 1) those more interested in psychosis (and/or the most severely or chronically mentally ill) and 2) those more interested in the neuroses and character disorders and general psychology. New external pressures to *widen* that split are currently with us in

several courts and state legislatures, where there have been, for instance, efforts to ensure that if and only if a mental illness has a demonstrable organic component should its treatment be covered by insurance. (An interesting dilemma.)

We need to work for good insurance coverage of *all* mental illness, as much as possible on a par with coverage of physical illness. Psychiatry that is interested only in psychosis is a retreat to the late nineteenth century and is—if somewhat tactically helpful for some patients in the short run—strategically unwise in the long run.

Along with welcome advances in neurobiology, psychopharmacology, genetics, etc. (advances that, I suppose, would have pleased and interested Freud), we must *retain* and document much of the large amount we have learned in psychology and psychodynamics, as well as in family and social psychiatry. We must help society use what we know, e.g., in *psychotherapy* but also in *prevention*, a politically difficult and vastly neglected field. We also need further advances in all of psychiatry, including better measurements of what we mean and what we do. And we need continued integration of bio-, psycho-, and social knowledge. Who is going to do this integration? Can we expect our trainees to do it if some of us do not do it well ourselves?

It is a relatively widespread human pastime to denigrate those who think differently or who know different things. It is usually relatively easy to stick to what we learned in the past and to be good at one field rather than two or three, and it is usually easier to simplify than to integrate. Some simplification, for a while, for a purpose, is often essential and productive in order to break down large complexity, to look at and measure component parts with relative clarity. But in a really complex field, like the brain plus the mind, with many interactive significant variables and very different levels of research access, continual back-and-forth motion between analysis and synthesis seems to me essential. So does some *extra* effort to study and measure what is *hard to study* and *long* to study, not just what is relatively easy and fast to quantify (and publish).

Psychiatry uniquely tries to include the extraordinary complexity of brain-plus-mind-plus-influences-on-brain-and-mind that results in health and illness. That is a difficult scientific field, constantly lively with simultaneously active physiological, psychological, and social variables. Clinicians know that and accept imperfect complex approaches and approximations and educated guesses and analogies: not just ideology or prejudice but educated guesses and regresses and syntheses and summaries, often nowadays based on considerable education not just in psychodynamics but in medicine, genetics, brain physiology, psychopharmacology, developmental psychology, family dynamics, and some sociology and anthropology.

That is clinical integration.

Many researchers, as opposed to clinicians, are impatient with much of this and for their good reasons want to isolate factors and measure crisp measurable units.

They have made and will make some brilliant advances in knowledge of the brain, but their knowledge is far from being all “hard,” and clinical knowledge is far from being all “soft.”

Psychiatry remains at some risk as a science and as an insurable medical specialty, partly because its complexity makes it a major example of a general problem in the accumulation of scientific knowledge: what is easiest to measure tends to get measured, published, and called “real” or “important”; what is harder to measure, even if as important or more important, gets measured far less and valued far less.

Good *long-term* or *integrative* studies are few. Good studies of psychodynamics and psychotherapy, for instance, are very few, and even those few tend to be relatively narrow and short-term—e.g., measuring change after 6 or 12 months. Someone recently calculated that to do good controlled studies of psychotherapy of the major *DSM-III-R* axis I diagnoses (leaving aside for the time being axis II and dual and plural diagnoses) would require decades and would cost tens of billions of dollars. That does not mean such studies are unimportant. But it does mean they probably will not be done. And that leaves us relatively vulnerable and open to being run by nonclinical simplifiers.

DSM-III and *III-R* and *IV* are part of the movement toward reliable categorization and measurement. They have helped many aspects of psychiatry, but they have harmed others, partly by oversimplifying. They emphasize clarity and reliability but, many clinicians think, sacrifice validity and the whole person. Signs of life outside *DSM-III-R* axis I seem to me to include a considerable list—e.g., persistent and not untroubled interest in axis II; in axes III, IV, and V; in possible additional axes; in commonplace and slippery comorbidity and dual or plural diagnoses; in the concept of reaction, as in posttraumatic stress disorders; in the currently semi-banished former emperor, psychodynamics; in development and adaptation as integral to diagnosis, especially in children and adolescents; in family and social stressors; and in protective factors. All these persist outside axis I. Life is complex. Clinicians do what they can and integrate what they can.

Integration and cooperation involve respect for colleagues and even for variety. It seems to me that many of us do not understand, or even much like, many of our colleagues. That is not entirely new, but its details change, and it may be worth some rethinking. Some psychiatrists and others now think of psychoanalysis as irrelevant, distracting, and passé. Some psychoanalysts and others think of 1991 psychiatry as hopelessly biologically reductionist. Some psychiatric residencies now hardly take psychodynamic psychotherapy seriously. (One resident in psychiatry was quoted nationally in print this year as saying something flamboyant like, “Now that psychoanalysis and analytic psychotherapy have been shown to be useless . . .”)

There are also value judgments and pressures from the public at large, from government, the media, pharmaceutical houses, insurance and managed care people,

and from large numbers of less (or differently) trained semicolleagues. Many of these represent or buttress strong economic forces and tend impatiently to push us to speed up and make cheaper. "Medicate a symptom" is in; "treat a patient" is out. Or, as an insurance executive asked, "Can't you listen faster?" All this, I think, is a challenge and means trouble, premature closures, danger of major losses, and danger of major oversimplifications.

The pressures are unlikely to change fast or be fixed fast or go away. But we can probably influence them, both as individuals and through our organizations. Much as I respect variety and private choices and cultivating one's own garden, I also want to suggest to everyone hearing this that it would probably be both useful and rewarding to devote some of your time, for a decade or two or three of your professional life, to public psychiatry—e.g., to psychiatric organizations and/or to the political, economic, public health, and preventive worlds *around* psychiatry.

Can psychiatry be integrated? Is each of us lost in our office or laboratory?

Let me call your attention briefly to two recent articles in the *American Journal of Psychiatry* that bear on biopsychosocial integration in interesting ways.

The first is the debate between Alan Stone and Gerald Klerman about the *Osheroff* case in the April 1990 issue of the *Journal* (1, 2)) (with follow-up letters to the Editor in the January and March 1991 issues of the *Journal* and letters to *Psychiatric News*). You will recall that the patient, Dr. Osheroff, a physician with a history of psychiatrists and psychiatric treatments that had included medication from a well-known psychopharmacologist, was admitted to Chestnut Lodge Hospital and treated for several months, for what was described as a mixed diagnostic picture, without antidepressant medication and without clear improvement. He then transferred to another hospital, was put on antidepressant medication, and improved rapidly. He sued Chestnut Lodge, saying that not promptly to have given him antidepressant medication was malpractice. The case was settled out of court and thus set no formal precedent. The Stone-Klerman debate about it poses some key questions about biological versus psychodynamic and milieu psychiatry, about reasonable practice guidelines, and about reasonable legal and clinical paths toward continued improvement and integration of psychiatric understanding and care. Should we ask *courts* to provide all-or-none "solutions" to our areas of clinical disagreement and choice? I agree with Dr. Stone that Dr. Klerman's essay, although it invites law to intrude, is not centrally about law but about Dr. Klerman's wish to "promulgate more uniform scientific standards of treatment in psychiatry, based on his own opinions about science and clinical practice" (2). Dr. Klerman's position in *Osheroff* would tend to introduce courts into clinical judgments and would not integrate but prematurely rigidify, and thus harm, our field. We can continually work to improve our standards and guidelines, but some of us—even experts—read some data differ-

ently from others. The legal idea that if a *respectable minority* would do something, it should be protected by law, is not at odds with science or with good clinical medicine; rather, the respectable minority idea will usually protect the continuing development of science and good clinical medicine and realistic integration.

As biological psychiatry predictably accumulates crisp and quantifiable data more quickly than psychodynamic and social psychiatry do—just look at our journals—we ought to work for more and better psychological and social research (as Dr. Klerman and others are well aware). But this whole area of bio- versus psychosocial argument will probably remain central to psychiatry and an area where we are at risk of major premature closures. One could call the risk intellectual and clinical segregation rather than integration.

The second recent *Journal* article bearing on integration that I suggest you consider is in the October 1990 issue, by Melvin Sabshin, on turning points in twentieth-century psychiatry (3). This historical overview is partly a tribute to Adolf Meyer, whose influential career in America in the second quarter of this century vigorously embodied and fostered biopsychosocial thinking and working—even if Meyer's usual term, "psychobiology," does not to me quite capture the important *social* edge of his and psychiatry's concerns. Sabshin calls our attention to some implications of various difficulties that psychiatry has had, and still has, in establishing its boundaries. He reminds us that there are major swings and trends in psychiatry over time, points to several, and predicts a resurgence of a complex variant of Meyerian psychobiology. I largely agree. I expect some will think him, or me, too analytic; others, too biological; and others, too optimistic. As to one nuance of difference between Dr. Sabshin and me, he tends to favor Meyer's word, "psychobiology," and I tend to favor Engel's word, "biopsychosocial." "Biopsychosocial" is such a familiar word for some of us that it may seem stale. Some of us are well-defended against it, although we may pay it lip service. Look at the word again. "Biopsychosocial" remains and should remain an essential word for psychiatry.

At this point in the several partial rehearsals for this talk that I have given around the country, I usually like to discuss two topics that are of lively concern to many APA members: 1) managed care and 2) the push by psychologists to gain hospital and prescribing privileges. I have mentioned both already, and, in the interest of time, I will not get into those areas today beyond one note on each.

On managed care, I note that discussions over the past few years are now increasingly being tied to interest in universal access to health care, and I think it is time for us to create universal access to health care for Americans.

And on psychologists, I will offer you a slogan that—perhaps because I live near Boston—appeals to me as reasonable: No medication without medical education.

I would like to end by saying a very few words that may join some of my interest in humane values and in-

tegration with some of Dr. Benedek's interests. I would like to talk a bit about children.

There was a flurry of publicity and noble sentiment for children's health at the United Nations in 1990. Much of it was fine publicity, and many national leaders came from around the world. It will probably be somewhat helpful. But there have been many flurries of publicity for children, even many so-called "days of the child" and many "weeks," "months," even "years" of the child. We can all be for children, and children make excellent propaganda. But as a long-term advocate for child health and mental health and someone who has taken part in some flurries of publicity, I am struck that children do far better in the speeches than in the funding and hard choices and work that are supposed to follow. We don't care for children as much as we say we do. *We don't care for children as much as we say we do.* And as I see it, this not caring has risen to a level that is a scandal.

Children don't vote. They are poor. They lack some mature political skills. They depend on others. And children are rarely desperately and immediately scary to adults—i.e., they are rarely mass murderers or major drug gangsters. They get hurt and grow with major pains and scars, and their troubles often show up terribly but gradually, complexly, for many years. Politicians, perhaps even more than ordinary adults, are rarely good at protecting long-term values as opposed to short-term results and publicity.

Leaving aside for the time being the many problems of children outside the United States, in the United States children have become our major *poverty* class. The New Deal and then the Great Society legislation of the 1960s and following years really did cause major changes in protection against poverty for *old* people in the United States—but that left children, and nowadays that often means children without what a previous generation might have called average, expectable, good enough parents.

The official poverty line in the United States is, of course, only an approximation, a guideline. But more than 20% of children in the United States live below the official poverty line. More than 20%, in this rich country. In cities, it is 30%. Minority children, of course, are especially likely to be poor: 39% of Hispanic children and 45% of black children.

Furthermore, leaving aside the hundreds of thousands of children with broken homes and troubled, abusing, or highly at-risk homes or family settings, the number of American children in our very flawed and unsafe system of *foster care* is 340,000 and growing; and the number of flatly *homeless* children in the United States is now estimated at around 200,000.

The Institute of Medicine recently issued a good report on research on mental disorders in children (4). It calculates that at least 12% of America's children—that is, at least 7.5 million youngsters—need treatment for a diagnosable mental disorder. Only a small fraction *get* treatment. The financial and human toll of this are staggering. Moreover, true cost figures are very much increased if lost lifetime productivity and other indirect

costs are taken into account—which they rarely are. Furthermore, the report's figure of 7.5 million youngsters seems to many of us probably too low, too conservative, and not fully able to grapple with the many ugly shades of gray of public child mental health that include poverty, violence, drugs, family disorder, and education failures.

A recent book about an urban slum, called *There Are No Children Here*, describes some current American childhood coping mechanisms. Mothers, for instance, are taking out burial insurance policies on their children, and children have learned to dive to the floor regularly "when shootings begin."

And adolescents? In 1990, a commission established by the American Medical Association and the National Association of State Boards of Education (a group of medical, education, and business leaders, including former Surgeon General Koop) reported on some of the profound physical and emotional health problems American teenagers currently have. On an average day, 135,000 students bring guns to school. The average American 16-year-old has seen approximately 100,000 acts of violence on television. Every year, about one million unwed teenage girls—about one in 10—become pregnant. The rates of births to unwed teenagers, most destined for poverty, have about quadrupled in the past 25 years. Every year, 2.5 million teenagers contract a sexually transmitted disease. More than a million are regular users of drugs beyond alcohol. Whereas traditional illnesses and public health problems usually let teenagers live, alcohol and other drugs and guns and violence increasingly do not. "Never before," the commission says, "has one generation of American teenagers been less healthy, less cared for, and less prepared for life *than their parents were* at the same age." The report points centrally to problems that are to a major extent behavioral and psychiatric: drinking, other drug use, sex-related problems, and violence.

This 1990 commission urged that teenagers be guaranteed access to health services, including mental health services, regardless of ability to pay. That would certainly help. But we ought also to realize that we know a lot more about prevention and education than we as a society are bringing to bear on our young people and on their and our future.

What kinds of priorities does our society have?

Thank you for listening.

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Elissa P. Benedek, M.D. One Hundred Nineteenth President, 1990–1991

Carolyn B. Robinowitz, M.D.

For those of us who were children in the 1940s, a special hero was Superman, not just because of his outstanding feats, but also because his prowess was hidden in the guise of “mild mannered reporter.” Elissa Benedek’s accomplishments and success in so many areas and her skilled blending of a full personal life with immense professional productivity are outstanding. As 119th President of APA, Dr. Benedek, in her thoughtful, quiet, yet firm manner, has led the Association extremely well in dealing with complexities and hardships and never losing sight of the goals for the field, for our patients, and for the children who *are* the future of our world. She hasn’t needed to go into a telephone booth to demonstrate her superpower. Even more, her ability to be remarkably effective, while avoiding being contentious, demonstrates a capacity to lead in the best sense of the word, that is, to enlist others’ active and enthusiastic support of her goals and objectives. This warm, assertive competence has marked not only her Presidential term, but Elissa Benedek’s life.

Dr. Benedek’s leadership potential, as well as her interest in young people, was apparent early. An honor student and an officer in student government, serious but fun loving, she was admired (and enjoyed) by teachers and peers alike. Throughout her childhood, Elissa was taught the value of education and service to others and was an acknowledged school leader. Her mother was an elementary school teacher, and her father a science teacher and principal. Both parents were respected and beloved by their students for their knowledge and their caring. These same attributes were noteworthy in their relations with their daughters. All four girls felt cherished and respected; each was regarded as a uniquely capable and extremely valuable person; and all were encouraged to set high standards and goals for themselves, to work to their fullest capacity, and to be actively concerned about others. There are two physicians: Elissa and Margo—who has combined subspecialization in endocrinology with development of new technology in medical products. Naomi, the youngest, runs a public relations firm, and Judy was an English teacher. The family is a close-knit one, and Elissa’s greatest sadness during her Presidential year was Judy’s

death from cancer. Typically, Elissa made frequent visits to Judy and her family in New York a high priority, while managing to maintain a full Presidential schedule and without burdening colleagues and associates with her pain.

Elissa Benedek was born in Detroit and received all of her education in the state of Michigan; her knowledge and capability testify to the excellence of her schooling at all levels. She completed her undergraduate and medical education at the University of Michigan in Ann Arbor. She had training in general psychiatry at the Neuropsychiatric Institute and in child psychiatry at the Children’s Psychiatric Hospital of the University of Michigan Medical Center.

She began and continued a productive academic career, rising rapidly through the ranks from instructor to become a full professor. Currently she is Clinical Professor of Psychiatry at the University of Michigan and Wayne State University. She is highly regarded as a clinician and teacher by students and faculty alike. Her loyalty to the university and its teaching is reflected in her needlepoint Michigan seals, but also in her undying support for school athletic activities—especially Michigan football.

Her major academic interests have been in education. Following a stint as administrator of a preadolescent boys’ inpatient unit, she became an Associate Director of Child Psychiatry and Training Director at the Center for Forensic Psychiatry, where she currently is Director of Research and Training, working with medical students, residents in general psychiatry, and fellows in forensic psychiatry.

The successful interweaving of personal and professional interests and activities is a prominent theme in her life. Courtship and marriage to Richard, an attorney, resulted in several aspects of collaboration (1–4). A modification of her work hours, to allow her to spend more time with her young children, led to informal training and considerable experience in forensic psychiatry. Over the years Dick and Elissa have worked together, focusing on the interfaces of law and psychiatry, particularly in the areas of divorce, child custody, and child abuse. Another, even more fruitful, result of collaboration has been their four children: David, Joel, Sarah, and Dina. These young people are extraordinary individuals, each unique, but each also mirroring the parents’ productivity. They provide a demonstration of their parents’ involvement, concern, and support. Family life has been important to the six of them, with mutual admiration and caring. Personal anecdotes demon-

Presented at the 144th annual meeting of the American Psychiatric Association, New Orleans, May 11–16, 1991. Dr. Robinowitz is Deputy Medical Director of APA. Address reprint requests to Dr. Robinowitz, APA, 1400 K St., N.W., Washington, DC 20005.

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strate gentle affection, humor and teasing, and praise and support and document the combination of goal-directed hard work and recreation. A particular family interest in camping brought teamwork and environmental experiences as well as fun. Parental enthusiasm for and pride in their children's education is reflected in photographs of numerous graduation ceremonies including David's recent graduation from the Uniformed Services University of the Health Sciences. A collaborator in child psychiatry studies with his mother (5, 6), David will begin a residency in psychiatry at Walter Reed Army Medical Center in July, demonstrating Elissa's success at conveying the excitement and attractiveness of our field.

I had the good fortune to meet Elissa, as so many women met, at the APA annual meeting in Dallas in 1972. A somewhat informal get-together of women psychiatrists became the basis for a number of friendships and work-based collegial relationships. For many, it was the first time that "women's issues" were given credence—hard to believe in today's society. The changing climate led to more visible interest. Over the next decade, Dr. Benedek published some important papers addressing these issues: the pregnant therapist, role integration of the psychiatrist-wife-mother, and the special concerns of the woman psychiatry resident (7–12). Her paper on editorial practices of journals documented problems of women in academia that persist, only partially addressed, almost 15 years later (13).

Dr. Benedek always has been concerned with the underprivileged and underserved. Her clinical and research interests in child psychiatry, the chronically mentally ill, sexually abused children and adults, victims of disasters and crime, and delinquents and their families, as well as offenders, all reflect her awareness of the needs of those whom society often avoids or denies. Her five dozen papers, six books, three dozen chapters, and 50 book reviews (at last count), in addition to numerous videotapes, cover a wide range of topics and emphasize the breadth of her knowledge and expertise. Her skills are broad based and include writing books for the public (in particular, two excellent books for children). The videotapes of her participation in mock trials are minicourses in forensic psychiatry, useful not only to the forensic specialist but to the general psychiatrist as well. Before her Presidential term, she had made nearly 200 presentations; her desire to communicate face to face with APA members has increased that number considerably.

Her committee work at APA began in 1972 when she became a member of the Task Force on Women in Psychiatry, which she then chaired. There, she was an advocate for women in the profession and for fulfillment of their potential, but avoided unnecessary confrontations and battles. The list of her committee responsibilities is almost endless, ranging from juvenile justice to judicial action, ethics to insurance, and national and international affairs. She served on the APA Board of Trustees as Trustee-At-Large, Secretary, and Vice-President before becoming President-Elect. She has

been a major resource in Michigan psychiatry as well. Her energy, skill, and leadership also were recognized by other groups. She was elected to a term on the Board of Directors of the Group for the Advancement of Psychiatry. At the Academy of Child and Adolescent Psychiatry she served on numerous committees—ethics, adolescence, children and the law, and program, as well as Project Future and was elected to its Council. The Michigan Council on Child Psychiatry elected her a Delegate to the Assembly of Regional Organizations of Child Psychiatry. A Fellow of the American College of Psychiatrists, she served on its committees on awards and membership, working to expand the representational base within the College, and was elected to a term on the Board of Directors. At the American Medical Association she has been a highly valued resource in studies of violence. She has been a consultant to a broad spectrum of community as well as professional groups including the President's Commission on Mental Health, Institute of Medicine, U.S. Secret Service, American Bar Association, and the government of Quebec. She is a senior examiner for the American Board of Psychiatry and Neurology. The list of her visiting professorships resembles a geography textbook, with presentations at numerous universities in this country and Canada. Her awards, too, are numerous and include many distinguished lectureships.

As President, she has been readily available to all, not just the important and influential. She has welcomed advice and criticism, avoiding "yes persons," sycophants, and isolation from real problems. She has been a leader of the people—encouraging others through her President's column in *Psychiatric News* to present their perspectives, concerns, and challenges. Mail and calls have been considered thoughtfully and responded to respectfully. Her legal experience has helped her consider the various sides and positions on issues, but her approach is not adversarial. She has been sensitive to members' concerns about conflicted or potentially divisive issues, but also has maintained her energetic course toward her goal: the best in patient care.

She has been especially interested in young people and minorities, working to bring them into leadership in the Association and supporting conditions for their empowerment in the community. Her Presidential appointments reflect a strong commitment to action, not just words, through greater involvement of underrepresented groups. This accessibility and awareness permeate her work relationships and friendships. Never too busy to consider an idea or direction, critique a document, or listen to personal problems and concerns, she also has been a thoughtful advocate for the staff, expressing appreciation for work as well as understanding of competing priorities. She has insisted that work include fun . . . and humor, noting that serious efforts and hard work do not demand a somber or depressed mood.

Elissa's thoughtfulness and sensitivity, intelligence, warmth, and gentleness have enabled her to address complex and difficult issues in a nonpolarizing manner and with "win-win" results. She seeks compromise and

comfort, but not at the expense of her objectives. This iron hand in a velvet glove has been an important adjunct in her relentless pursuit of her theme, "Our Children: Our Future."

Last year, in her response to Dr. Pardes' Presidential address, she quoted the prayer of Benjamin Rush that began his book *Medical Inquiries and Observations Upon the Diseases of the Mind*. He said,

I feel as though I am about to tread on consecrated ground. I'm aware of the difficulty and importance of it and most humbly implore that being whose government extends to the thoughts of all its creatures to so direct mine in this arduous undertaking that nothing harmful to my fellow citizens may fall from my pen and that this work may be a means of lessening the proportion of some of the greatest evils of human life. (14, p. 9)

This prayer expressed her Presidential wish, her "sentiments for the strength and wisdom to lead our organization in a direction that lessens the proportion of evil and illness in human life" (15).

I have been fortunate to have such a warm, caring, and steadfast friend to whom I could turn for both personal and professional advice, direction, and support. More to the point, we all have benefited from her concerned and effective leadership and vision for the future.

Her Presidential wish has been fulfilled, and, by dint of her remarkable efforts, she has worked to improve life for us, our patients, families, and generations to come. She is a woman for all seasons and settings.

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Body Dysmorphic Disorder: The Distress of Imagined Ugliness

Katharine A. Phillips, M.D.

***Objective:** Body dysmorphic disorder, a preoccupation with an imagined defect in physical appearance, has a rich tradition in European psychiatry but has been largely neglected in the United States. Because this little-known disorder is probably more common than is generally realized and can have profound consequences, the author reviews its history, clinical features, and possible relationship to other psychiatric disorders. **Data Collection:** Data sources consisted of the MEDLINE database and relevant references in articles obtained from this search. Of 145 articles and books obtained, 100 were selected for inclusion in this review on the basis of how closely they conformed to the concept of body dysmorphic disorder as defined in DSM-III-R and how substantially they contributed to an understanding of the disorder's history, clinical features, or nosologic status. **Findings:** Body dysmorphic disorder has been colorfully described in the European literature for more than a century. Although its concerns might sound trivial, this disorder can lead to social isolation (including being housebound), occupational dysfunction, unnecessary cosmetic surgery, and suicide. The most commonly associated psychiatric disorder appears to be depression. Although a definitive treatment does not exist, preliminary evidence suggests that serotonergic antidepressant medications may be useful. Whether body dysmorphic disorder is related to other psychiatric disorders, such as psychosis, mood disorder, social phobia, or obsessive-compulsive disorder, is unclear at this time. **Conclusions:** More research on the nosology, clinical features, and treatment response of body dysmorphic disorder is important, given the distress and impairment this often secret disorder can cause.*

(Am J Psychiatry 1991; 148:1138–1149)

Body dysmorphic disorder, a preoccupation with an imagined defect in physical appearance, has a rich tradition in European psychiatry but is largely unknown in the United States (1). It is in fact new to DSM-III-R. This little-known disorder, however, may be

more common than is thought, can cause severe distress and impairment, and may be treatable.

The disorder's essential feature, as defined in DSM-III-R, is a preoccupation with some imagined defect in appearance in a normal-appearing person; or, if a slight physical anomaly is present, the concern is grossly excessive. Patients may complain, for example, of "devilish-looking" eyebrows (1), an excessively large nose (2) or head (3), small genitals (4), or a "stretched" mouth (5)—supposed deformities that patients feel are unbearably ugly. This preoccupation can be persistent and pervasive, leading to social withdrawal as well as repeated visits to dermatologists and plastic surgeons in an attempt to correct the imagined defect.

Case 1. A 28-year-old single white man became preoccupied at the age of 18 with his minimally thinning hair. Despite

Presented in part at the 143rd annual meeting of the American Psychiatric Association, New York, May 12–17, 1990. Received July 13, 1990; revision received Dec. 31, 1990; accepted Jan. 28, 1991. From McLean Hospital and the Department of Psychiatry, Harvard Medical School, Boston. Address reprint requests to Dr. Phillips, McLean Hospital, 115 Mill St., Belmont, MA 02178.

The author thanks Drs. Harrison G. Pope, Jr., James I. Hudson, Kerrin White, John G. Gunderson, Kazuhisa Nakao, and Ralph S. Albertini for their comments on this manuscript and Drs. Pope, Hudson, Nakao, Gianni L. Faedda, Daniel Perschonok, and Venyamin Pinsky for their translation of foreign-language articles.

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reassurance from others that his hair loss was not noticeable, he worried about it for hours a day, becoming “deeply depressed,” socially withdrawn, and unable to attend classes or do his schoolwork. Although he could acknowledge the excessiveness of his preoccupation, he was unable to stop it. He saw four dermatologists but was not comforted by their reassurance that his hair loss was minor and treatment unnecessary. The patient’s preoccupation and subsequent depression have persisted for 10 years and have continued to interfere with his social life and work, to the extent that he avoids most social events and has been able to work only part-time as a baker. He only recently sought psychiatric referral, at the insistence of his girlfriend, who said his symptoms were ruining their relationship.

This case illustrates some common features of body dysmorphic disorder as well as the *DSM-III-R* criterion that the belief not be delusional in intensity (“the person can acknowledge the possibility that he or she may be exaggerating the extent of the defect or that there may be no defect at all”). *DSM-III-R* also requires that the disorder not occur exclusively during the course of anorexia nervosa or transsexualism.

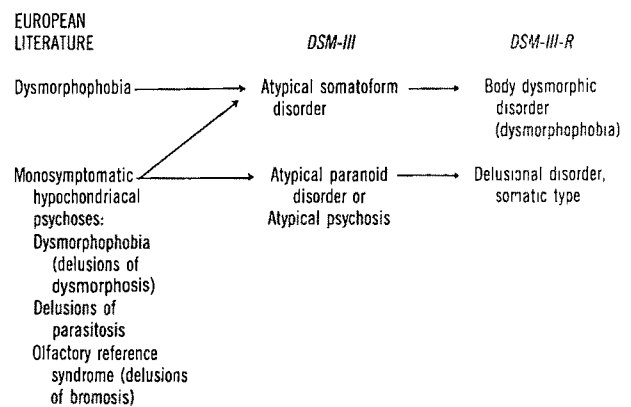
Now that body dysmorphic disorder has a place in psychiatric nosology, it seems worthwhile to review what is known about this disorder. This review will discuss the history and clinical features of body dysmorphic disorder and its possible relationship to other psychiatric disorders, including psychosis, mood disorder, social phobia, and obsessive-compulsive disorder.

HISTORY

Body dysmorphic disorder is a new name for an old syndrome. It has long been described in the European, Russian, and Japanese literature under a variety of names, most commonly “dysmorphophobia,” a term coined by Morselli 100 years ago (6). Although the term “dysmorphophobia” has been used in different ways (7), it has generally been defined as a subjective feeling of ugliness or physical defect that the patient thinks is noticeable to others, despite a normal appearance (8, 9). According to Philippopoulos (10), this term comes from *dysmorfia*, a Greek word meaning ugliness, specifically of the face, and first appeared in the *Histories* of Herodotus referring to the myth of the “ugliest girl in Sparta,” who was taken to a shrine each day by her nurse so she might be delivered from her homeliness.

Kraepelin (11) and Janet (12) are among the turn-of-the-century European psychiatrists who described a dysmorphophobic syndrome. Kraepelin believed that the persistent, ego-dystonic nature of dysmorphophobic symptoms warranted its classification as a compulsive neurosis. Similarly, Janet classified the *obsession de la honte de corps* (obsession with shame of the body) within a large class of syndromes similar to obsessive-compulsive disorder. Janet believed that this concern was relatively common, if one looked for it, and he emphasized the extreme shame experienced

FIGURE 1. Evolution of Disorders Related to Body Dysmorphic Disorder



by these individuals, who feared being “ugly and ridiculous.”

The psychoanalytic literature contains a classic case of dysmorphophobia—the “hypochondriacal paranoia” experienced by the Wolf-Man (13). This patient, who had previously had a compulsive neurosis analyzed by Freud, “neglected his daily life and work because he was engrossed, to the exclusion of all else, in the state of his nose” (its supposed scars, holes, and swelling). “His life was centered on the little mirror in his pocket, and his fate depended on what it revealed or was about to reveal” (13). Psychoanalysis suggested that his nose represented his penis and that he desired to be castrated and made into a woman; his symptom was also thought to reflect an identification with his mother, in part because its onset occurred soon after seeing a wart on her nose.

“Beauty hypochondria” (*Schönheitshypochondrie*) and “one who is worried about being ugly” (*Hässlichkeit-skümmerer*) are similar concepts, used by Jahrreiss in 1930 and discussed later by Ladee (14). Ladee captured some of the central qualities of body dysmorphic disorder in his description of beauty hypochondria: “the preoccupation is so exclusively centered on one aspect of the bodily appearance, which is experienced as deformed, repulsive, unacceptable or ridiculous, that the whole of one’s existence is dominated by this preoccupation and nothing else has any significance any more.” The features of greatest concern were the nose, teeth, skin, and hair. “Dermatologic hypochondriasis” (15) is another term used to describe a body-dysmorphic-disorder-like syndrome that focuses on “defects” of the skin and hair.

In 1949, Stekel (16) wrote about “the peculiar group of compulsive ideas which concern the body. There are people who occupy themselves continuously with a specific part of the body. In one case it is the nose; in another it is the bald head; in a third case the ear, the eyes, or (in women) the bosom, the genitalia, etc. These obsessive thoughts are very tormenting.” Although in the European literature dysmorphophobia and its equivalents generally referred to a nondelusional concern, the term was also used to describe a preoccupation of delu-

sional intensity. As such, it was also classified as one of the monosymptomatic hypochondriacal psychoses (17, 18) (figure 1). These psychotic disorders consist of a single delusional belief of a somatic nature, usually in the absence of other prominent psychotic symptoms, and are thus similar to delusional disorder, somatic type, in *DSM-III-R* (18, 19). The other two common monosymptomatic hypochondriacal syndromes are delusions of parasitosis (the belief that one is infested with parasites or other vermin) and olfactory reference syndrome, or delusions of bromosis (the belief that one emits an offensive body odor) (17). This psychotic version of dysmorphophobia has also been called "delusions of dysmorphism" (17).

Despite its clear presence in the European literature, dysmorphophobia is not included in *ICD-8* or *ICD-9*. Less surprising is its absence from *DSM-I*, *DSM-II*, and the Research Diagnostic Criteria (20), since this disorder was only rarely mentioned in the U.S. literature.

Dysmorphophobia first entered U.S. psychiatric nosology in *DSM-III*—but only as an example of an atypical somatoform disorder and without diagnostic criteria. Its delusional and nondelusional versions were not differentiated, the delusional version having no clear place in *DSM-III*. It, too, might have been diagnosed as atypical somatoform disorder (21, 22) or perhaps as atypical psychosis (23) or atypical paranoid disorder (21), the last reflecting similarities between monosymptomatic hypochondriasis and Kraepelin's concept of paranoia (19).

Dysmorphophobia was accorded separate diagnostic status in *DSM-III-R*, which calls it body dysmorphic disorder and notes that "dysmorphophobia" is a misnomer because the disorder does not involve phobic avoidance (24). Dietrich (25), however, justified the use of "dysmorphophobia" on the basis of patients' fear of ridicule and of upsetting others with their ugliness. Unlike *DSM-III*, *DSM-III-R* differentiates nondelusional body dysmorphic disorder from delusional disorder, somatic type (a new type of delusional disorder in *DSM-III-R*), its delusional counterpart, which is classified as a psychotic disorder. Although differentiating a delusional belief from the nondelusional thinking of body dysmorphic disorder can be extremely difficult (26–29), some authors (30, 31) have stated that this distinction is important because it may have treatment implications.

To my knowledge, only five articles on body dysmorphic disorder (4, 7, 32–34) have been published since its appearance in *DSM-III-R* in 1987, suggesting that this disorder continues to receive little attention in the American literature.

CLINICAL FEATURES

The clinical features described here are based not only on the scant literature on body dysmorphic disorder itself but also on the more ample literature on conditions that generally conform to this disorder's defini-

tion—primarily dysmorphophobia. Many cases of delusional dysmorphophobia are described in the literature on monosymptomatic hypochondriasis and delusional disorder, somatic type; although delusional dysmorphophobia is not the focus of this review, many of its major references are included because it can be difficult to distinguish clinically from body dysmorphic disorder as defined in *DSM-III-R*.

This review is based largely on case reports and small case series. It is limited by the lack of clear, operationalized definitions of dysmorphophobia and similar syndromes in the literature. This is particularly problematic for the sizable literature on psychiatric aspects of cosmetic surgery (35), which includes many uncontrolled studies of patients seeking such procedures as breast augmentation (36) and rhinoplasty (37, 38). Because psychiatric disorders in these studies are generally not rigorously diagnosed, it is unclear how many and which patients have body dysmorphic disorder; therefore, most of these studies are omitted from consideration here. This review focuses on those studies and cases which appear to meet *DSM-III-R* criteria for body dysmorphic disorder.

Phenomenology

Patients with body dysmorphic disorder are intensely preoccupied with an imagined or grossly exaggerated defect in some aspect of their appearance, regarding it with "loathing, repugnance, and shame" (17), sometimes to the point of being "tortured" by their concern (10) and unable to think of anything else (8). Most commonly, complaints involve facial flaws (39), such as wrinkles (8, 28, 40), spots (24, 29), scars (12), vascular markings (4), acne (15, 16, 41, 42), paleness (4, 15, 24) or redness (43–45) of the complexion, swelling (45–47), facial asymmetry or disproportion (15, 39, 45, 47, 48), excessive facial hair (3, 12, 15, 29, 43, 49), or hair abnormalities such as thinning (15, 16, 49), with an accompanying fear of impending baldness (14, 16, 29, 50). Other common preoccupations include the shape, size, or some other aspect of the nose (2–6, 13, 14, 16, 24, 25, 28–30, 33, 39–41, 43, 45, 47, 48, 51–56), eyes (12, 16, 40, 41, 45, 48, 52, 54), eyelids (39, 45), eyebrows (1, 8, 39, 57), ears (29, 43), mouth (5, 8, 48), lips (43, 58), teeth (14, 45), jaw (1, 12), chin (1, 6, 8), cheeks (1, 45, 47, 59), or head (3, 25, 39).

Any other body part can be the focus of concern, including the genitals (4, 8, 25, 29, 41, 60), breasts (2, 8, 14, 16, 24, 25, 54, 56), buttocks (8, 12), abdomen (56), arms (8, 12), hands (6, 12, 14), feet (12), legs (8, 52), hips (43), shoulders (4, 14), spine (56), or skin (14, 33, 61).

Although the complaint is often specific, it may also be notably vague (15) or difficult to understand (39)—for example, a "funny and crinkly nose" (28) or "the skin under my eyes joins my nose in a funny way" (62).

Individuals with body dysmorphic disorder may be preoccupied with different body parts at different times (4, 12, 29, 39, 43, 56) or with several simultaneously (1, 4, 24, 28, 39, 43, 47, 52, 56, 63)—for example, both

a double chin and "chipmunk cheeks" (1). Unlike patients with anorexia or transsexualism, they do not have a disturbance of the body image as a whole (64, 65).

Demographics

Although the prevalence of body dysmorphic disorder is unknown, it is probably not rare (12, 59, 66), contrary to Morselli's belief that it was an uncommon disorder (6). Fitts et al. (32) attempted to estimate its prevalence in a nonclinical population and found that 70% of 258 college students reported at least some dissatisfaction and 46% reported some preoccupation with an aspect of their appearance; 28% appeared to meet all criteria for the disorder. However, this finding is likely to be an overestimate of body dysmorphic disorder's prevalence because anorexia nervosa and concern with weight alone were not excluded, and the diagnosis was made by an apparently unvalidated self-report questionnaire that used broad criteria. In psychiatric clinical samples, it would seem that body dysmorphic disorder is likely to be underrepresented and underdiagnosed because of patients' secrecy about their symptoms and their reluctance to seek psychiatric treatment (40). In fact, psychiatrists probably see only a small fraction of patients with this disorder, most of whom consult dermatologists, internists, or plastic surgeons (27).

The ratio of women to men in reported cases is approximately 1.3:1, although 62% of the subjects in a Japanese series of 274 dysmorphophobic individuals who sought cosmetic surgery were male (39). Most individuals with body dysmorphic disorder are unmarried; 85% of the subjects in case reports of individuals 19 years old or older were single. Age at onset is usually from early adolescence through the 20s (1, 27, 39, 45); 19 is the mean age in reported cases, but patients wait a mean of more than 6 years before seeking psychiatric treatment.

Premorbid Features

Several authors, generalizing from case reports and small case series, have suggested that a variety of personality traits may predispose to body dysmorphic disorder. Those commonly cited are obsessive-compulsive (1, 5), schizoid (1, 5, 15, 52), narcissistic (1, 5, 52), or a mix of these (1). Individuals with body dysmorphic disorder may also be premorbidly perfectionistic (1, 8, 43, 52), self-critical (8), insecure (47), sensitive (5, 6, 8, 28, 33, 43, 47, 57, 67), shy or reserved (1, 5, 8, 45, 53, 56, 64), and asthenic or hyposthenic (15).

In a case-control study of 17 patients with dysmorphophobia, Hay (8) noted that the disorder seemed to be rooted in a sensitive or insecure personality. Similarly, Fukuda (39), on the basis of a large series of dysmorphophobic surgical patients, suggested that the disorder occurs in individuals with Schneiderian insecure and asthenic personality types as well as the sensitive subtype. Zaidens (15), however, believed that, premorbidly, her 12 patients with dermatologic hypochondria-

sis (which is not defined but seems equivalent to body dysmorphic disorder) were unusually attractive individuals with latent schizophrenia.

A clear premorbid profile does not emerge from these reports. More systematic assessment is needed, with a focus on the differentiation of premorbid from comorbid features.

Associated Features

Frequent mirror checking, which can consume many hours a day and can be extremely disrupting and difficult to resist, is a common associated feature of body dysmorphic disorder (1, 3, 4, 10, 13-15, 28, 29, 34, 40, 41, 43, 45, 51, 52, 54, 56, 60). However, some patients avoid mirrors in an often unsuccessful attempt to diminish their distress and preoccupation (4, 43, 64). Other associated behaviors include excessive hair combing (3) and hair removal (29).

Individuals with body dysmorphic disorder are often concerned that others may be looking at, talking about, or mocking their "defect" (1, 8, 16, 24, 28-30, 33, 39, 40, 43, 45, 47, 54, 62-64). Consequently, they may try to camouflage it with makeup (4, 43), their hands (2, 5, 8, 24, 43, 46), their hair (2, 3, 43, 64), or a hat (2, 64) or other clothing (8, 12, 43); or they may constantly raise "devious-looking" eyebrows or jut forward a "receding" jaw (1). They may also frequently compare their "ugly" body part with that of others (8, 16, 29) or repeatedly seek reassurance that they look normal, to no avail (54). They sometimes bring photographs of themselves to their treater to prove the hideousness of their appearance (40). Ironically, they may be completely unconcerned with a coexisting real and substantial physical abnormality (43, 52).

Psychiatric disorders associated with body dysmorphic disorder run the gamut of psychiatric syndromes. Because prospective studies are lacking, it is not clear whether the following disorders predispose to or are caused by body dysmorphic disorder or simply coexist with it, without a causal link.

The associated disorder most often mentioned is depression (4, 5, 8, 15, 16, 28-30, 33, 43, 47, 53, 56, 57, 60). In Cotterill's series of 16 dysmorphophobic dermatology patients (29), five were depressed and two attempted suicide, making depression the most common associated disorder. In another dermatology series (67), five of 12 patients with dysmorphophobia were moderately or severely depressed, compared with none of the comparison subjects (who were healthy or had psoriasis), and the patients with dysmorphophobia scored significantly higher as a group than the comparison subjects on the Beck Depression Inventory. Most reports imply that body dysmorphic disorder causes the depression.

Hay (8), however, using several psychometric scales and Schneiderian nosology, found that only one of 17 subjects with dysmorphophobia was depressed but that 11 had a severe personality disorder (Schneiderian sensitive and insecure types) and five were schizophrenic

(although four of these had a bodily concern of delusional proportions). Compared with control subjects, the subjects with dysmorphophobia were "severely disturbed" in that they were more introverted, "obsessoid," neurotic, and hostile. Connolly and Gipson (9), who studied 187 patients 15 years after they had had rhinoplasty, found that significantly more of the patients who had sought surgery for esthetic reasons (many of whom were considered dysmorphophobic) had schizophrenia (six of 86) than did those who had corrected an actual deformity due to disease or injury (one of 101). Others have also reported the coexistence of body dysmorphic disorder and schizophrenia (15, 29, 39, 40, 45, 47, 63) or psychosis (41), although the definitions of schizophrenia that were used may have been overly broad and thus included individuals who would now be diagnosed as having mood, personality, obsessive-compulsive, or other disorders.

Obsessive-compulsive disorder is also associated with body dysmorphic disorder (3, 4, 8, 41, 43, 47). In one series of eight patients with severe obsessive-compulsive disorder, three also had body dysmorphic disorder (3). Hay (8), as already noted, found subjects with dysmorphophobia to be more "obsessoid" than control subjects, and Hardy and Cotterill (67) found that subjects with dysmorphophobia ($N=12$) and control subjects with psoriasis scored higher on the Leyton Obsessional Inventory than did healthy control subjects, a finding of unclear significance.

Social avoidance and isolation (12, 15, 53, 54, 60), introversion (39), avoidant personality disorder (33), dissatisfaction with relationships (49), and shame and low self-esteem (2, 24, 41, 42, 46, 53) may also coexist with body dysmorphic disorder, as may anxiety (4, 10, 15, 42, 43, 45, 56, 57, 60), olfactory reference syndrome (45), "compulsive eating" (15), and anorexia nervosa (42, 68). In one case (59), anorexia nervosa was secondary to the body dysmorphic disorder: the patient severely starved himself because he feared his cheeks were "too rosy and round."

The frequency of comorbid body dysmorphic disorder and these various syndromes is unknown. Prospective studies using operationalized criteria and structured interviews are needed to assess a broader range of psychopathology longitudinally and to attempt to differentiate premorbid, comorbid, and outcome conditions.

Course

Little is known about the course or outcome of body dysmorphic disorder (1, 28). It appears that the body part of concern may shift over time (4, 12, 43) and that the preoccupation may progress to delusional thinking (4, 8). A few authors reported waxing and waning or even resolution of the disorder (although they did not specify the relationship of course to treatment) (45, 54). However, most reported cases suggest that, without treatment, body dysmorphic disorder usually persists for at least several years, if not decades, and that the

symptoms tend to be unremitting, sometimes worsening over time (41, 63).

Impairment and Complications

The literature consistently emphasizes the suffering and impairment that can be caused by body dysmorphic disorder. Difficulties in social, marital, and occupational functioning can result (2, 4, 28, 30), to the point where the patient's life can be "profoundly disrupted" (27). One woman with "facial swelling" stopped going to school to avoid being seen by others (46), and another woman dangerously sped through red lights on her motorcycle so that others could not see her "excessive" facial hair (43). A young man dated only small, slight women, thinking his "small" penis would not be so noticeable to a woman of smaller build (8). As these cases suggest, such behavior is often due to embarrassment over the imagined defect, which can lead to avoidance of dating or sexual contact (8, 15, 29, 46, 56), working (2, 13, 15, 29, 30, 33, 43, 45), attending school (10, 28, 34, 40, 44, 45, 51), shopping (28), swimming (8, 43, 64), and other activities. Substantial social isolation (2, 8, 25, 29, 33, 34, 40, 43, 44, 46, 47, 59, 60, 64), including being housebound (15, 28, 29, 45), may result.

Functional impairment can also result from the inordinate amount of time that some patients spend with their preoccupation, which leads to a neglect of other aspects of life. This is illustrated by one woman who spent up to 8 hours a day cutting her hair to make it symmetric (4) and by another who spent most of the day examining her face with a magnifying glass for excessive facial hair (29).

The distress of body dysmorphic disorder can be so severe that it causes suicidal ideation (5, 16, 29), suicide attempts (8, 25, 28, 29, 56), and suicide (41, 45, 59, 60).

A specific complication of body dysmorphic disorder is a request for unnecessary plastic surgery (1, 2, 4, 8, 14, 16, 28, 39-41, 43, 47, 51, 52, 54, 59, 60, 64). In fact, this disorder may account for an estimated 2% of all patients who request plastic surgery (1, 39). These patients may go from one surgeon to another requesting such procedures as rhinoplasties, facelifts, mandibular augmentation for "weak" or receding jaw lines, or eyebrow elevation until they find one willing to operate (1, 39). After surgery, they may become even more preoccupied with the same defect, sometimes leading to multiple operations (39, 41, 56), or they may focus on a new defect (39, 56), as did one patient, who after four rhinoplasties became preoccupied with his waist, thinning hair, and sloped shoulders (4). As Andreasen and Bardach (1) stated, some patients eventually become "synthetic creations of artificial noses, breasts, ears, and hips."

Individuals with body dysmorphic disorder also consult medical specialists other than surgeons, often dermatologists, requesting such treatments as electrolysis or a skin or hair transplant (4, 13, 29, 40, 44, 45, 54, 61). They are rarely reassured by normal physical examination results and rarely satisfied with treatment.

Family History

Hollander et al. (4) assessed five patients with DSM-III-R-diagnosed body dysmorphic disorder and found a family history of mood disorder in two (both of whom had personal histories of mood disorder) and obsessive-compulsive disorder in two (one of whom had a personal history of obsessive-compulsive disorder). Other scattered case reports document family histories of mood disorder (1, 8, 28, 46, 47, 57) or schizophrenia (5, 29, 33, 45, 47), with approximately half the patients having the disorder themselves. Zaidens (15) observed "a preponderance of marked neurotic behavior and more than average psychotic behavior" in family members. However, some patients with body dysmorphic disorder have no family history of psychiatric disorder (8, 34, 47). A family history of body dysmorphic disorder has not been reported; whether this reflects patients' and family members' secretiveness or a lack of familial transmission is not clear.

Although these family history data do not establish a familial pattern or clearly link body dysmorphic disorder with any other psychiatric disorder, they do raise the question of an association with mood disorder, obsessive-compulsive disorder, and broadly defined schizophrenia. Systematic assessment of family history in a larger number of cases is needed. Also needed is careful documentation of coexisting diagnoses in probands because these diagnoses are often not reported and could account for the presence of disorders other than body dysmorphic disorder in family members.

Biological Markers

A nonsuppressed response to the dexamethasone suppression test was reported in a patient whose concern about his small genitals, diagnosed as delusional disorder, somatic type (21), may have been body dysmorphic disorder. This patient was dysthymic but did not have major depression or other psychiatric disorder. Although this finding is provocative and raises the question of a relationship between body dysmorphic disorder and mood disorder, no other such cases have been reported. A normal sleep EEG was obtained in one case (46).

Etiology

Speculations on the etiology of body dysmorphic disorder range from theories about the defense mechanism of displacement to those involving neurotransmitter dysfunction. From a psychological perspective, some authors suggested that body dysmorphic disorder arises from the unconscious displacement of sexual or emotional conflict or feelings of inferiority, guilt, or poor self-image onto a body part (2, 16, 24, 54, 57). Similarly, bodily symptoms may defend against a weak identity (52) or reflect an underlying ego deficit and disturbance in interpersonal communication (69). Body dysmorphic disorder may also reflect an attempt to

manage social or communication deficits (61), "liberate" one from a need to contend with the outside world (54), or explain one's suffering (52) or one's failures with the opposite sex (2).

Several authors suggested that the chosen body part may be symbolic of another body part—for example, the nose may represent the phallus (13, 14, 16, 62, 70, 71) and may, as such, symbolize impotence (53). Some patients may identify the chosen body part with that of another person (70), often a parent (2, 13).

Philippopoulos (10) suggested that a woman's fear of being ugly and repulsive might cover up an unconscious urge to yield to sexual temptation—her "ugliness" allowing her to reject the "feminine role" she unconsciously wishes for. Others (14, 71) suggested that incestuous wishes and castration anxiety are unconscious motives in the development of symptoms.

"Unharmonious" family backgrounds (14) and "unfavorable" childhood experiences producing enduring feelings of being unloved, insecure, and rejected (2, 53), as well as teasing about bodily appearance (2), have been invoked as contributing factors. Ladee (14) postulated the importance of "an extreme, highly ambivalent dependence on one of the parents, usually the mother, for whom physical beauty was important" and who then "applied this criterion of evaluation to the child." Some individuals secretly envy and compare themselves with their more attractive siblings, with whom their parents may also compare them (2, 24).

Several investigators postulated that an acute precipitating factor may trigger the onset of symptoms, such as a chance remark about the body part of concern (10, 29, 51, 57)—for example, "You certainly resemble your father" (1), "You look very nice but you have got a small mouth" (8), or "Why is your face half red and half white?" (44). Hay (8) reported that such a remark was at least partly responsible for the onset of symptoms in nine of his 17 patients. Several case reports noted the sudden onset of symptoms soon after a distressing life event, such as a spouse's affair or abandonment by a boyfriend (54).

The dramatic physical and physiological changes of adolescence may also play a role in body dysmorphic disorder's development (1). Zaidens (15), writing from a psychoanalytic perspective, believed that minor skin changes of adolescence, such as the development of mild acne, could trigger symptoms; she theorized that such a skin change further damages the "vulnerable ego" of an individual with latent schizophrenia, causing collapse of a self-esteem overly dependent on physical attractiveness. The resulting "hypochondriasis" functions as a "protective cover-up" to allay anxiety.

Body dysmorphic disorder is rarely associated with organic mental syndromes (27), although some authors (5, 8) by definition excluded body image disturbances of an organic etiology from their definition of body dysmorphic disorder. One report (72), however, suggested that a case of dysmorphophobia with associated neurological abnormalities may have been caused by subacute sclerosing panencephalitis.

As already noted, some authors have stated that body dysmorphic disorder is rooted in certain premorbid personality types (73). Others postulated that it may be a variant of other psychiatric disorders, such as mood disorder, schizophrenia, social phobia, or obsessive-compulsive disorder. As such, body dysmorphic disorder would be expected to share etiologic sources with these disorders, which would implicate the contribution of biological abnormalities.

The etiology of body dysmorphic disorder is most likely complex. As Olley (2) suggested, the "motivations are diverse and a unitary explanation unlikely."

Treatment

Uncertainties about the etiology of body dysmorphic disorder are reflected in the diversity of its treatments, which include medication, psychotherapy, behavioral therapy, and cosmetic surgery.

A number of case reports described the resolution of body dysmorphic disorder with antidepressants. The greatest number of successful outcomes has been reported for the serotonin-reuptake blockers clomipramine (four cases) and fluoxetine (two cases) (4), although clomipramine was ineffective in one case (34). In most of these cases, symptoms of body dysmorphic disorder had previously been refractory to a variety of somatic treatments. Of note, clomipramine and fluoxetine successfully treated symptoms that at times seemed delusional (4), and clomipramine has effectively treated the delusional, body-dysmorphic-disorder-like symptoms of monosymptomatic hypochondriasis (74) and delusional disorder, somatic type (21).

Successful response has also been reported (one case for each) for imipramine (47), imipramine plus anti-anxiety agents (47), imipramine plus amitriptyline (3), tranylcypromine (46), and a combination of trimipramine, phenelzine, and perphenazine (3). However, most reported outcomes with these and similar medications—imipramine (4, 5, 28, 46, 47), trazodone (4), and unspecified tricyclics and monoamine oxidase inhibitors (4, 29, 34)—have been negative. Lack of response has also been reported for lithium (4), alprazolam (4), diazepam (43), and unspecified benzodiazepines (34). ECT has been largely unsuccessful (4, 8, 28, 41, 43, 75); only one good response has been reported (8).

Negative medication findings are difficult to evaluate because they may have been due to inadequate dose or duration of treatment, which in most cases could not be assessed on the basis of the information provided.

For those patients who responded to antidepressant medication, concurrent depression was reported in fewer than half; both the body dysmorphic disorder and the major depression resolved in three cases, and the body dysmorphic disorder alone resolved in one. No patients who responded to antidepressants had concurrent obsessive-compulsive disorder.

Successful outcomes were maintained with continued treatment for the duration of the reported follow-up, which ranged from 4 months to 3 years. However,

symptoms did recur in patients whose medication was decreased or discontinued (4).

Antipsychotics have been largely ineffective. Negative results have been reported for loxitane (46), trifluoperazine (28, 33), thioridazine (4, 33), flupenthixol (75), pimozide (29), and unspecified agents (4). However, one patient had a partial response to pimozide (4), and one responded to a combination of an unspecified neuroleptic and antidepressant (47).

Some authors recommended behavioral therapy (28) or supportive psychotherapy (15) but did not provide evidence for their efficacy. Documented outcomes with these approaches have been mixed. Behavioral therapy has produced both unsuccessful (3, 34) and successful results, the latter with exposure therapy (43), audiovisual self-confrontation (48), and systematic desensitization (44). Psychoanalysis, psychoanalytic psychotherapy, and supportive psychotherapy have also been both ineffective (4, 16, 29, 34, 56, 76) and effective (10, 13, 41, 57, 61, 71). Unfortunately, many of the ineffective treatments were not described in detail, making it difficult to assess their adequacy.

Plastic surgery is yet another option. Only a few reports refer to clearly dysmorphophobic patients, and these have mixed results (5, 30, 38, 40, 41, 51, 54, 55, 77, 78). Some authors suggested that certain patients with minimal deformity may have a good outcome but emphasize the importance of psychiatric screening before surgery (78). However, Fukuda (39) stated that most patients refuse psychiatric consultation and that it is risky to operate on them because their expectations for surgery are often unrealistic and they are often dissatisfied with the results, escalate their complaints, and bear grudges against the physician. Andreasen and Bardach (1) also stated that because their real "defect" is emotional rather than physical, individuals with body dysmorphic disorder are rarely fully satisfied with surgical results and often find a new "defect" in need of correction. Ladee (14) warned that cosmetic surgery—especially rhinoplasty in men—may have an adverse outcome because it can "meet the need for self-punishment, masochism and passive desires" and "can unleash such unbridled aggressions in response that either the patient himself or sometimes the doctor becomes the victim thereof." To avoid such adverse outcomes, collaboration of psychiatrists with dermatologists (50, 79) and plastic surgeons (39, 78, 80, 81) is recommended in the evaluation and treatment of patients seeking elective cosmetic surgery.

Finally, one case report (8) documented improvement in body dysmorphic disorder after a modified leukotomy.

No clear consensus emerges regarding the treatment of choice for body dysmorphic disorder—except that it should in most cases be psychiatric, not dermatologic (50) or surgical (1, 62, 82). Unfortunately, patients with body dysmorphic disorder tend to resist psychiatric referral and treatment (1, 10, 27, 39, 62, 80). Most authors would probably agree with Stekel's admonition (16) that "the physician should not attempt to remove [body dysmorphic disorder] by reasoning. It will be useless."

Although a definitive treatment does not exist at this time, preliminary evidence suggests that several antidepressant medications—perhaps, in particular, the serotonin-reuptake blockers—may be useful for at least some patients and therefore worth trying. In addition, the antipsychotic pimozide has been recommended because of its success, in uncontrolled studies, in treating monosymptomatic hypochondriasis and delusional disorder, somatic type (19), which can be difficult to distinguish clinically from body dysmorphic disorder (26–29); however, it has also been suggested that this medication is not useful in clearly nondelusional patients (17, 29, 30). The usefulness of behavior therapy and psychotherapy is unclear, but de Leon et al. (33) suggested that attention to psychosocial factors—as well as use of medications—is essential. Certainly, much remains to be learned about the treatment of this complex disorder.

DISCUSSION

Body dysmorphic disorder has been described for more than a century and seems to identify a particularly distressed group of individuals whose preoccupation with a “defect” in their appearance can lead to social and occupational dysfunction as well as unnecessary surgery. However, it is remarkable how little is known about this disorder. Despite its substantial historical tradition, empirical work has been largely limited to case reports and small case series. The reason for this neglect is not clear. One contributing factor may be the omission of body dysmorphic disorder, until recently, from official diagnostic systems. Perhaps even more important, this is often a secret disorder: many individuals with body dysmorphic disorder keep their concerns to themselves because they feel them to be so profoundly humiliating and embarrassing. In addition, if these individuals seek treatment, they often do so outside the mental health system.

Certainly, the validity and utility of the diagnosis of body dysmorphic disorder would be strengthened by the study of more patients, who may be easily available if the disorder is looked for. Also useful would be the application of operationalized diagnostic criteria to select patients and standardized instruments to assess comorbidity, systematic assessment of family history and treatment response, careful identification of the intensity of belief and degree of actual deformity, and prospective evaluation.

Although it is generally implied that body dysmorphic disorder is a psychiatric disorder in its own right, a few authors have suggested that it is instead a nonspecific symptom that can occur in a variety of psychiatric syndromes (8, 39, 52, 83) or that it can be either (27, 45). Thomas (5, 84) highlighted this distinction by differentiating between primary and secondary dysmorphophobia: primary dysmorphophobia is equivalent to the discrete syndrome of body dysmorphic disorder and secondary dysmorphophobia is a nonspecific symp-

tom of a variety of underlying psychiatric disorders such as schizophrenia, depression, monosymptomatic hypochondriasis, anorexia nervosa, and severe neurosis. However, Hollander et al. (85) stated that there is no evidence to support such a dichotomy and noted that their patients responded to the serotonin-reuptake blockers fluoxetine and clomipramine regardless of the “primary” or “secondary” nature of their body dysmorphic disorder symptoms, casting doubt on the validity of this distinction.

The classification of body dysmorphic disorder as a somatoform disorder is presumably based on the patient’s concern with somatic complaints as well as the disorder’s historical association with hypochondriasis (86). However, empirical evidence for an association with the somatoform disorders is lacking (23). For example, other somatoform disorders, such as conversion disorder and hypochondriasis, have not been described as comorbid with body dysmorphic disorder or present in family members of patients with body dysmorphic disorder.

Indeed, many authors have argued that body dysmorphic disorder is related to or a variant of one of the nonsomatoform disorders, including the psychoses, mood disorders, social phobia, and obsessive-compulsive disorder. Some have implied that it is merely a symptom of one of these disorders and thus not a distinct diagnostic entity in its own right, but most suggest that it is a separate diagnostic entity which nonetheless shares features and perhaps etiologic sources with one of these other disorders.

The strongest support for a link between body dysmorphic disorder and psychosis comes from the early European literature, where body dysmorphic disorder was in fact often classified as a psychotic illness (monosymptomatic hypochondriasis). In particular, many earlier authors considered body dysmorphic disorder a prodrome or variant of schizophrenia (9, 15, 40, 45, 87), which has been reported to coexist with body dysmorphic disorder and to occur in family members of probands without schizophrenia themselves. However, although body dysmorphic disorder may sometimes appear to be of delusional intensity, core schizophrenic symptoms are usually absent. In addition, the concept that body dysmorphic disorder is a variant of schizophrenia is weakened by undefined and probably overly broad uses of the term “schizophrenia.” Finally, the generally poor response to neuroleptics of body dysmorphic disorder reported further weakens the evidence for a connection with schizophrenia and other psychotic disorders, although it does not rule out such a connection.

A link between mood disorder and body dysmorphic disorder has little historical tradition but some preliminary empirical support. Body dysmorphic disorder appears often to coexist with mood disorders, and it sometimes responds to antidepressant medication, even in the absence of concurrent depression. In addition, a family history of mood disorder exists for some probands with body dysmorphic disorder who have no

past or concurrent mood disorder themselves. This suggests that body dysmorphic disorder rather than mood disorder in the probands may explain the presence of mood disorder in some family members, strengthening the evidence for a link between body dysmorphic disorder and mood disorder. On the other hand, the apparent poor response of body dysmorphic disorder to ECT somewhat weakens the evidence for its relationship to mood disorder.

In the Japanese and Korean literature (51, 88), body dysmorphic disorder is considered a subtype of a larger group of disorders (*Taijin-Phobia* in Japan) that closely resembles *DSM-III-R* social phobia or, similarly, avoidant personality disorder, reflecting a focus on body dysmorphic disorder's interpersonal aspects. Indeed, some of the premorbid, associated, and complicating features of body dysmorphic disorder already noted resemble aspects of these two disorders. However, the Japanese and Korean literature classify many patients with body dysmorphic disorder as having "severe" social phobia, a type of social phobia with not only obsessive and phobic but also some delusional characteristics, which does not fit neatly into any *DSM-III-R* category (51, 88). Although body dysmorphic disorder appears to share an early age at onset and often chronic course with social phobia (89) and avoidant personality disorder, further research is needed to determine whether these disorders share other features, such as similar comorbidity, family history, or treatment history.

Several early authors, including Morselli (6), Kraepelin (11), and Janet (12), suggested that body dysmorphic disorder is related to obsessive-compulsive neurosis. More recently, Tynes et al. (90) have proposed such a link, and Rapoport (91) has described "somatic obsession-compulsion," a type of obsessive-compulsive disorder involving a "preoccupation with part of [the] body," such as large ears, which sounds similar to body dysmorphic disorder. Weak empirical evidence comes from the previously described psychometric work of Hay (8) and Hardy and Cotterill (67). Stronger, although preliminary, support comes from more recent case reports of coexisting obsessive-compulsive disorder in probands, family history of obsessive-compulsive disorder in patients with body dysmorphic disorder but not obsessive-compulsive disorder, similar age at onset and similar course, and possible preferential response to the serotonin-reuptake blockers clomipramine and fluoxetine.

In addition, body dysmorphic disorder symptoms seem phenomenologically similar to obsessional thinking—they are persistent, distressing thoughts that are intrusive and difficult to ignore or suppress. Some patients with body dysmorphic disorder have compulsive, ritualistic behaviors—such as frequent mirror checking—that are designed to diminish their anxiety but may not be successful (28). However, several authors (33, 34, 92) have suggested that the symptoms of body dysmorphic disorder are more akin to overvalued ideas than obsessions: the thoughts seem more natural than

intrusive, are acquiesced to without much resistance, and are held with an intense (although nondelusional) conviction rather than regarded as senseless—although these features are also characteristic of some patients with obsessive-compulsive disorder (93).

In a more speculative vein, body dysmorphic disorder may be more like obsessive-compulsive disorder than the somatoform disorders in that body dysmorphic disorder usually involves a private, inner torment rather than the more public suffering of patients with, for example, hypochondriasis or somatoform pain disorder, which usually actively aim to involve others. As Kenyon (86) stated, "These patients [those with dysmorphicophobia] wish to appear normal but feel that others notice that they are not, whilst hypochondriacs want to draw attention to themselves by saying they are not normal."

At this time, the evidence for a relationship with obsessive-compulsive disorder seems most convincing—at least for some cases of body dysmorphic disorder—but is preliminary. As Hollander et al. (4) have pointed out, although their findings raise the possibility of a common pathogenesis between body dysmorphic disorder and obsessive-compulsive disorder, they do not exclude the possibility of a relationship with mood disorder. In addition, Hudson and Pope (94) recently proposed that obsessive-compulsive disorder itself is a form of "affective spectrum disorder."

The relationship of body dysmorphic disorder to delusional disorder, somatic type, and, similarly, to monosymptomatic hypochondriasis merits special attention. Although it might be clinically important to try to differentiate these two disorders (31), this may at times be difficult, if not impossible (21, 26–29, 33). Instead, body dysmorphic disorder and delusional disorder, somatic type, might be conceptualized as lying along a spectrum of severity, or intensity of belief, in which body dysmorphic disorder's preoccupation or overvalued ideation (with some insight) shades imperceptibly into the delusional thinking of delusional disorder, somatic type, with a hazy area of overlap. Indeed, *DSM-III-R* states that it is unclear whether body dysmorphic disorder and delusional disorder, somatic type, can be distinguished or are instead variants of the same disorder. Several authors have argued for the latter view, stating that dysmorphicophobia encompasses both psychotic and nonpsychotic (or neurotic) conditions (16, 24, 40, 47, 54, 63) or, similarly, that it may be variously expressed as a preoccupation, an obsession, an overvalued idea, or a frank delusion (27, 62). In support of this view, nondelusional body dysmorphic disorder symptoms may at times become delusional and, when delusional, may still respond to antidepressant medication alone (4). Similarly, despite the suggestion that delusional disorder, somatic type, and monosymptomatic hypochondriasis may best respond to pimozide (18), several case reports described the resolution of these disorders with antidepressant medication (21, 22, 74, 95), further blurring the distinction between delusional and nondelusional disorders. These

findings are in keeping with the belief of Hollander et al. (85) that body dysmorphic disorder criteria should be broadened to include symptoms of both a delusional and nondelusional nature.

Although the overlap of body dysmorphic disorder with delusional thinking might seem to imply a link with psychosis, it is also compatible with a link with obsessive-compulsive disorder because a similar spectrum has been proposed for this disorder, with severe obsessions being of delusional proportions ("obsessive-compulsive psychosis") (3, 96). If body dysmorphic disorder is related to obsessive-compulsive disorder, it and delusional disorder, somatic type, might be similarly related along an obsessive-compulsive continuum from more to less insight, resistance, and dystonicity (4, 21). Or, as already noted, body dysmorphic disorder may in fact encompass the entire spectrum, subsuming both nondelusional and delusional thinking.

Questions also arise about the other end of this putative spectrum of severity—in particular, how does body dysmorphic disorder differ from normal concern with physical appearance? Similar boundary problems exist for other psychiatric disorders, such as the differentiation of depression from normal grieving. However, the boundary of body dysmorphic disorder with normalcy may be particularly fuzzy because concern with physical appearance is nearly universal and might even be considered a hallmark of normal adolescence. Indeed, the study by Fitts et al. (32) found that 70% of a college sample was at least somewhat dissatisfied with some aspect of their appearance, and many subjects in other nonclinical samples have been shown to have at least a mildly distorted body image (97, 98). In addition, cultural factors influence how the body is viewed and how much attention and concern its imperfections receive (52, 62, 99). Despite the almost certain existence of a hazy area of overlap between normal and abnormal concern, however, there clearly is a group of people who are excessively preoccupied, severely distressed, and often substantially impaired by their concern about a minimal or nonexistent deformity, suggesting that bodily preoccupation in this extreme form can and should be distinguished from normal concern.

Many mysteries remain. Where should the line between normal and abnormal concern be drawn? Is body dysmorphic disorder a separate diagnostic entity? What is its relationship to other psychiatric disorders? Are some other seemingly similar disorders related to, or variants of, body dysmorphic disorder—for example, olfactory reference syndrome, erythrophobia (fear of blushing), and koro (complaints of genital retraction)? At this time, these questions have no conclusive answers. However, until clarifying evidence emerges, it does seem that body dysmorphic disorder should remain a separate diagnostic category: although it bears some resemblance to obsessive-compulsive disorder, its clinical features are unique and not easily subsumed by any other psychiatric category.

Whether body dysmorphic disorder and its delusional counterpart should remain separate disorders is

an equally complex question that requires further research. Body dysmorphic disorder and delusional disorder, somatic type, do appear to overlap in several important ways—not only in terms of their historical classification but also in terms of their symptoms, course, and, possibly, treatment response. In addition, it is often extremely difficult, if not impossible, to determine into which of these categories a given preoccupation falls. On the basis of these similarities and diagnostic conundrums it would seem, as Hollander et al. (4) suggested, that the criteria for body dysmorphic disorder should be broadened to subsume both disorders—that is, to include not only nondelusional but also delusional symptoms.

These diagnostic dilemmas will become disentangled only by further research, such as that currently in progress (100). Systematic assessment in different clinical populations of the phenomenology, comorbidity, age at onset, course, family history, biological markers, and treatment response of body dysmorphic disorder may provide useful clues as to how this disorder should be classified—as a somatoform, psychotic, mood, or anxiety disorder. Even more important, such data are needed to guide clinicians in recognizing and treating this potentially disabling disorder and, eventually, to shed light on its etiology.

In the meantime, it seems important to attempt to identify these individuals—many of whom may be found in obsessive-compulsive disorder, mood disorder, dermatologic, and surgical populations—because they may respond to psychiatric treatment and might help them avoid unnecessary cosmetic surgery. However, finding these patients may require vigilance and persistence on the clinician's part because many are extremely embarrassed by their "ugliness" and may be reluctant to reveal their concern, even to treaters they have known for years.

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Psychodynamics of Suicide, With Particular Reference to the Young

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***Objective and Method:** The article reviews the literature on the psychodynamics of suicide, focusing on factors that will help in evaluating and treating the young suicidal patient. Articles published in refereed journals and books and book chapters based on such articles are the source of most of the material. Articles that first brought a new finding to notice are given preference. Methodological limitations and contradictions with the data of other studies are pointed out. **Findings:** The psychodynamic meaning of suicide for a patient derives from both affective and cognitive components. Rage, hopelessness, despair, and guilt are important affective states in which young patients commit suicide. The meanings of suicide can be usefully organized around the conscious (cognitive) and unconscious meanings given to death by the suicidal patient: death as reunion, death as rebirth, death as retaliatory abandonment, death as revenge, and death as self-punishment or atonement. **Conclusions:** Knowledge of the psychodynamics helps to distinguish which patients with any given diagnosis are at risk for suicide. Such knowledge is essential to the psychotherapeutic treatment of the young suicidal patient. Topics for future research include the role of anxiety in suicide; the capacity to bear hopelessness, rage, and other unpleasant affects without regression; the use of particular defense mechanisms in distinguishing the risk of either suicidal or violent behavior; and the relation of specific psychodynamic conflicts seen in suicidal patients to particular psychiatric diagnoses.*

(Am J Psychiatry 1991; 148:1150-1158)

In the past few decades, patients with depression, alcoholism, and schizophrenia have been shown to have a high risk of suicide (1-4). More recently, panic disorder has been linked to a high frequency of attempted suicide (5). The vast majority of patients in any of these categories, however, are not suicidal. Nor does suicide seem to be simply a symptom of an underlying diagnostic condition that goes away if the condition responds to treatment. The current revival of interest in the psychodynamics of suicide derives in part from the increasing realization that assigning to a patient a diagnosis that has a high risk of suicide is not in itself an explanation for suicide.

As a consequence, attention has focused on differentiating the factors within any diagnosis that distinguish patients who are suicidal from those who are not (6-10) and on the lethal factors that cross traditional diagnostic boundaries. Contemporary biological research into

suicide moves largely from this starting point (11, 12), as does contemporary psychodynamic interest (13).

The high rate of youth suicide has been the subject of particular concern. "Youth" generally refers to the period of transition between adolescence and adulthood, ending at the age of 30 (14). Although the rise in youth suicide since 1958 appears to have peaked now, the rate remains high. There is demographic evidence that the rate of youth suicide is related to the relative percentage of young people reaching adulthood at a particular period, with the recent rise being the result of the maturation of the "baby boom" generation born after World War II (15, 16). Epidemiologists also point to an increase in the incidence of depression among young people during the same period (17). Advances in establishing diagnostic as well as psychosocial factors of vulnerability serve to underline the importance of understanding the psychodynamics of youngsters who are suicidal when the majority of those with comparable risk factors are not.

Psychodynamics, as used in contemporary psychiatry, deals with the quality of interpersonal relations, recurrent conflict patterns, and, ultimately, the *meaning* of actions and experiences (18, 19). Such meaning is understood by observing both its affective and its cognitive components.

Presented in part at the 143rd annual meeting of the American Psychiatric Association, New York, May 12-17, 1990. Received June 20, 1990; revision received Jan. 7, 1991; accepted Jan. 28, 1991. From the American Suicide Foundation. Address reprint requests to Dr. Hendin, American Suicide Foundation, 1045 Park Ave., New York, NY 10028.

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AFFECTIVE STATE

It is helpful to begin by understanding the affective state or states in which the patient commits suicide, partly because the affective state usually clarifies and structures the cognitive one. Although suicide is often loosely described as an escape, in young patients it is usually an escape from an intolerable affective state. Rage, hopelessness, despair, and guilt are some of the emotions that have been shown to predominate in suicidal patients. The nature and intensity of these affects are indicators that distinguish patients who are suicidal from those who are not (7, 20–24).

Rage

Clinical study of seriously suicidal young, urban black subjects indicated that among this population the problems of suicide, rage, and violence were related (22, 23, 25–28). Suicide was usually the outgrowth of a devastating struggle to deal with conscious rage and conscious murderous impulses originating in early personal exposure to violence. For example, one young man who eventually killed himself had been trapped as a boy in a room with his father, who was engaged in a shootout with the police. The father, although wounded, continued to fire with a small arsenal until he was killed. As a teenager this young man came to admire Hitler's ability to kill millions. He was arrested for violent fights and wrestled with the idea of knifing his mother and brother before attempting suicide. What he found most disturbing about his violent behavior was the loss of control that he experienced when enraged; he thought he might enjoy killing if he could do it in a cool, controlled, detached manner (22, 23).

The origin of youthful rage in a violent family situation (22, 23, 25–28) that produced identification with a parent or parental surrogate who was violent, self-destructive, or both is typical of young black persons of both sexes who commit suicide. They are disturbed by the feeling of being overwhelmed by loss of control over angry homicidal impulses, and what they describe seems to be a fear of ego disintegration. Their concern is less with the consequences of their violence than with the feeling that they cannot predict or control their impulsive rage and that it threatens their capacity to function. Suicide can be a form of control exercised by people who feel torn apart by rage and violence (22, 23).

The interrelation of rage, violence, and suicide is not limited to young black people. Individuals who have killed others have a suicide rate several hundred times greater than those who have not (13, 29). This rate is largely the result of murder followed quickly by suicide, which is more frequent among white people than it is among the black population (29). In a recent review of studies of the relation between suicide and violence (30), it was estimated that about 30% of violent individuals have histories of self-destructive behavior, while about 10%–20% of suicidal persons have histories of violent behavior. Psychological autopsies of

young suicide victims indicated that just under one-half of them had histories of aggressive and antisocial behavior, a much higher rate than that of older age groups, while only one-quarter had histories of major depressive disorder, a much lower rate than has been found in older populations (31). With nonviolent patients as well, the open expression of hostility and rage distinguishes depressed patients who are suicidal from those who are not (6).

Hopelessness, Despair, and Desperation

Beck et al. (7) found that the seriousness of suicidal intent was correlated less with the degree of depression than with one particular aspect of depression: hopelessness about the future. They observed high suicidal intent in some patients who showed minimal depression but whose expectations for the future were also minimal. Eighty-nine of 207 patients hospitalized because they were contemplating suicide had high ratings on a measure of hopelessness from the Beck Depression Inventory. In the subsequent 5 years, 14 of the 207 patients committed suicide. Thirteen of these 14 were from the group of 89 who had the high ratings on the measure of hopelessness. A variety of diagnoses were given the patients who ranked high on hopelessness, but one-half were diagnosed as having some form of depression.

Clinicians often use the word “despair” rather than “hopelessness” to convey the emotional state distinguishing suicidal patients from patients who are depressed but not suicidal. Despair has been described as developing from aloneness, murderous hate, and self-contempt (21) or, more generally, as resulting from any state that leads to the individual's “inability to maintain or envision any human connections of significance” (32).

My own experience with a handful of patients seen a few days before their suicides suggests that their affective state was closer to desperation than to hopelessness or despair. Many patients who feel despair or are hopeless about the future are resigned to their situation. Desperation implies not only a sense of hopelessness about change but a sense that life is impossible without such change. Anxiety and urgency are an integral part of this affective state. The importance of these affective elements was confirmed in a recent study by Fawcett et al. (33) of patients with major affective disorder, among whom anxiety was a stronger predictor of short-term risk of suicide than was hopelessness.

Guilt

In a recently completed study of suicide and posttraumatic stress disorder (PTSD) in Vietnam veterans (24), of 100 veterans with PTSD, 19 had made suicide attempts and 15 more were preoccupied with suicide. Guilt about actions committed in combat, usually involving the killing of civilians and most often while feeling out of control, was the variable that best explained

their suicidal behavior. These actions had taken place when these men were 19 years of age on average, but their guilt persisted and fueled their suicide attempts and actual suicides. Their nightmares were often filled with images in which they were punished in ways that reflected their actions in Vietnam.

For the vast majority of the suicidal veterans, the actions that had been committed were of such a nature that the postservice guilt, self-hatred, and nightmares of punishment seem understandable and almost inevitable. In a few cases, however, the combat actions were equivocal, and some were combined with guilt about surviving when close friends had not. When things went well at work or in personal relations, the surviving veterans tended to feel they had no right to be enjoying what their friends who died could never enjoy, and they acted in ways that sabotaged their own success.

The guilt seen in Vietnam veterans was usually conscious, but at times it was only suspected from their behavior and became evident when they discussed their dreams, fantasies, and associations. Consciously expressed, excessive or inappropriate guilt is considered to be one of the cardinal symptoms of a major depressive episode. Such guilt may be elaborated in a delusional way, focused on ideas of sin or worthlessness. Depressed patients who are delusional have been shown to be far more likely to kill themselves than those who are not; the delusions have not been found to be the outgrowth of a greater degree of depression (8).

COGNITION AND MEANING

The cognitive component of the meaning of suicide helps clarify the affective aspects of the suicidal act. For example, the guilt of a veteran about his combat actions and his view of suicide as a punishment that he deserves contribute in a complementary way to our understanding of his suicide attempt. As Kernberg (34) aptly pointed out with regard to the affect of hopelessness, "In clinical practice the question is not the patient's general feeling of 'hopelessness' but what, concretely, the patient is hopeless about."

"Cognition" generally refers to conscious ideation, while "meaning" includes both conscious and unconscious affects and perceptions. The meanings of suicide can be usefully organized around the conscious and unconscious meanings given to death by the suicidal patient.

The evidence for determining any such meaning should not be limited to information the patient volunteers or to his or her responses to questions. The meanings of suicide are often unconscious and are best elicited by free association and dreams. Serious suicide attempts usually stimulate dreams; two-thirds of the suicidal patients in a study by Raphael (35) remembered dreams from the period prior to their attempts. Patients who do not recall such dreams will often do so under hypnosis (36). Those who have studied the dreams of patients shortly before or after

suicide attempts have found that the dreams were invariably helpful in understanding the motive for suicide (35-38). Eliciting the dreams of suicidal patients is an important part of a psychiatric evaluation (38), much as it is in cases of PTSD. The dreams of acutely suicidal patients are similar to those of patients with PTSD in the minimal extent to which unconscious material is disguised (35).

We have learned that suicidal patients give to death a special meaning, using death in their adaptation to life. A critical aspect of this adaptation is their actual or fantasized use of their own deaths in an effort to control others or to maintain an illusory control over their own lives.

Some of the common meanings given to death by young patients who have committed suicide are death as reunion (36, 39-43), death as rebirth (36, 39-43), death as retaliatory abandonment (36), death as revenge (43, 44), and death as self-punishment or atonement (24, 36, 45, 46).

Rebirth and Reunion

Some suicidal patients cherish fantasies of effecting a rebirth or a reunion with a lost object through suicide. Death is attractive to these patients as more than simply an escape from crises. In a case that I reported previously (36), for example, a young woman jumped in front of a subway train and was severely injured. Her suicide attempt was precipitated by the end of one of her many unhappy and complicated love relationships and by the vacation of her therapist, both of which events she related to the abandonment of the family when she was a child by her father, whom she idealized. In a dream about her suicide attempt, she was in a long, narrow tunnel. In the light at the end of it, she saw a man and woman standing over a manger. In her associations to the dream, the tunnel suggested to her the subway where she jumped and the way in which the train came out of the tunnel and into the lighted platform area. Moving from the darkness of the tunnel and into light brought to her mind the process of birth. She saw the man and woman as her father and mother. The child in the manger was both the Christ child and herself. (She particularly identified with the idea that death united Christ with his father.) She saw her life as set on a course in which gratification of her fantasies was only possible through her death. One can see how much this patient accomplished in her death fantasy. She is reborn into an intact family, is reunited with her father, and, finally, is omnipotent. For a patient with such fantasies, the thought of dying has become more tolerable.

Early in this century, Ernest Jones and Carl Jung recognized the importance of rebirth and reunion fantasies in suicidal patients. Jones (39) suggested that such fantasies had as their prototype the wish to return to the mother's womb, while Jung (40) and his followers emphasized the unconscious need for spiritual rebirth. This dynamic was reemphasized in the 1930s by Zilboorg (41), who wrote that "the drive towards death, always with

the flag of immortality in hand, carried with it the fantasy of joining the dead or dying or being joined in death."

Pollock (42), writing several decades later, emphasized the suicidal person's regression to a state in which there is little differentiation of self and object. The suicide victim gives himself or herself up to an undifferentiated "supposedly blissful state of reunion." This state of narcissistic fusion or symbiotic union with a powerful figure is said to overcome the dread of death and accounts for the patient's fantasies of grandiosity and immortality.

Pollock believed that what may seem to be identification of the suicidal person with someone who is dead is simply likely to be "reflective of the wish to reunite with the one from whom the separation occurred" (42). His view is somewhat different from that of Hendrick (47), who described the suicide of depressed persons as the consequence of identification with a lost object, in contrast to suicide—usually by schizoid or schizophrenic individuals—in which identification with someone who is dead is the purpose of dying and represents fulfillment of the identification.

Retaliatory Abandonment

Suicide attempts and the possibility of suicide give some people the illusion of mastery over a situation through their control of their living or dying. This is probably why some of them keep the means for suicide readily available, whether or not they ever attempt to kill themselves.

In a case described previously (36), a college student was seen following a serious suicide attempt, which he barely survived. The attempt was precipitated by his rejection by a male friend to whom he was sexually attracted and without whom he felt life was intolerable. Shortly after the suicide attempt, the patient had a dream in which he was working for the United Nations, where he had an office that encompassed the entire first floor of the UN building. He was interviewing one of his friends who was applying for a position, and after reviewing the friend's qualifications, he finally told him that he did not qualify for the job. This patient accomplished the same goal in the dream and in the suicide attempt: through being the one who rejects or leaves he gains illusory control over an interpersonal relationship. His holding an important position and having a large office in the dream strongly suggest that he also experienced a feeling of omnipotent mastery through death.

Revenge

Freud's view of suicide derived from his observation that depression is an attempt to regain through introjection a lost object that is both loved and hated (48). In depression, the hate originally directed toward the object becomes displaced onto the internalized representation of the object. The hated person, now identified with the self, can be destroyed by destroying the self. In Freud's formulation, suicide expresses a re-

pressed wish to kill an ambivalently regarded lost love object, and thus it is ultimately an act of revenge.

The mechanism was seen as primarily unconscious. Although the depressed Viennese patients described by Freud were not violent, and we still see patients similar to his, hostility is often strikingly conscious when young people use suicide as an expression of revenge toward their parents. Such youngsters usually feel overwhelmed by murderous feelings toward their parents and are even fearful that they may act on them. These feelings may be conscious as well as expressed in dreams. The suicide may be precipitated by some immediate frustration followed by an impulsive response. However, these youngsters, even if they seem to have been functioning well, invariably have histories of being increasingly unable to cope with murderous rage toward their parents.

Such an expression of revenge was the suicide of a 15-year-old girl who was doing well in school, was well liked by her many friends, and was said by her parents to have shown no evidence of problems. She shot herself in the head with a gun belonging to her father after a fight with her parents over their refusal to allow her and a friend to go to an amusement park some distance from their home. Sessions with the parents after her death revealed that there were long-standing problems between the girl and her mother. After the suicide, her grandmother told the parents that the young woman had told her a day or two before the suicide that she dreamed she had killed her mother. Shortly before killing herself, she told a friend that suicide would be a way of getting back at her parents.

Self-Punishment or Atonement

In the classical formulation of suicide as the product of unconscious hostility toward an introjected lost love object, guilt about hatred of the object is the source of the need for self-punishment. In destroying oneself and the object, one accomplishes atonement as well as revenge.

In 1948 in an article on suicide, Elizabeth Kilpatrick (49) wrote, "When we understand narcissism not as love of the self, but as love of the idealized image of the self, we become aware of the gravity of self-hate and alienation which needs to be present." She pointed out that the unconscious idealized self-image is often accompanied by its counterpart, a despised self-image. This view is maintained in contemporary object relations theory, which formulates suicide as an attempt by the superego, with which the good self is identified, to eliminate the bad self (50).

After Bibring (51) in 1953 focused attention on depression as an independent primary affect—"the emotional correlate of a partial or complete collapse of the ego since it feels unable to live up to its aspirations"—greater attention was paid to suicide as a form of punishment or atonement for such failure. Haim (45) in 1974 noted the "peculiarities" in the organization of the "ego ideal" in adolescents who are prone to suicide,

describing an "archaic megalomaniacal ego ideal" with a "demand for the absolute" and "absence or inadequacy of reshaping when put to the test of reality." Mack (46), in his description of the life and suicide of an adolescent girl, viewed her suicide as largely the result of an inability to live with an ego ideal affected by early damage and low self-esteem and the impossibility of satisfying her mother's need to fulfill through her the mother's own need for perfection.

Suicide has been mentioned as a self-inflicted punishment by Vietnam veterans guilty about actions in combat. Comparable dynamics are seen in civilian life (perhaps with less frequency today than heretofore) in young people who, having been raised in fundamentalist religious families, are in anguish over their failure to fulfill moral expectations. They tend to regard their drinking, fighting, or other antisocial behavior as sins and to view suicide as a form of expiation. Their dreams in connection with suicide attempts often contain images of hellfire and brimstone (52). In psychotic individuals these ideas are expressed as delusions of sin.

More common in psychiatric practice today are young people who feel they have failed to meet their own and their families' academic, vocational, and social aspirations and have fallen short of matching the achievements of their siblings and peers. Their lives are filled with a sense of failure and humiliation, their dreams frequently center on "having missed the boat" (52), and their suicides are often an expression of self-hatred and a need for punishment. A typical case is that of a 20-year-old patient who committed suicide after he recorded this dream in his diary: "I was back at high school and saw familiar faces. I felt embarrassed and humiliated. They were going on with life. I tried to be incognito but was spotted." In a similar vein he wrote, "When I think of myself as a recovering patient, I am more patient with myself and more willing to change things. When I compare myself to my potential, I mourn."

INTERRELATED MEANINGS

Although these dynamic themes have different significance in different patients, they are not mutually exclusive. Both the dependent and the aggressive aspects of suicide can be active in some patients, as Melanie Klein (53) recognized when she wrote, "In some cases the fantasies underlying suicide aim at preserving the internalized good objects and that part of the ego which is identified with good objects, and also at destroying the other part of the ego which is identified with the bad objects." At times the self-punishment resulting from self-hatred seems to have become an end in itself, but there is usually evidence in suicide of "a double aim of first cleansing the self, and then uniting (actually reuniting) with an omnipotent love object" (54). Whether the aim is to cleanse or to rid oneself of the "bad part," purification achieved by either exorcism or self-punish-

ment is seen as enabling the individual to hope that he can be loved by a significant object once again.

A theme that may run through the varying psychodynamic meanings of suicide is the perception of suicidal patients, experienced unconsciously and/or consciously, that they are already dead. Dreams of death, dying, coffins, and burial are frequent in suicidal young people (32, 35), who experience emotional death in their attempts to bury their rage and despair. The preoccupation of some with death is often the climax of having felt emotionally dead for a lifetime (55).

All of the psychodynamic meanings given to death by suicidal patients can be conceptualized as responses to loss, separation, or abandonment. Rebirth and reunion fantasies may be seen as attempts to undo or deny such losses. Becoming the one who leaves is one way to avoid the feeling of having been left. Feelings of rage that are repressed, suppressed, or expressed may derive from the experience of loss. Self-punishment may express guilt at having been responsible for a loss and the fantasy of rapprochement through atonement. Even numbness or deadness and the insistence that one is already psychologically dead may reflect determination not to live without the lost object (13, 56). Although suicidal patients may have in common their use of their own deaths to deal with their losses, the various meanings they give to their deaths account for the variety in the psychodynamics of suicide.

For most suicidal patients, however, a rejection of life usually includes a rejection of the parents from whom it originated (13, 43, 56). The patient is likely to feel in a deep way that he or she was abandoned first (13, 56). In this sense Freud's insight into the relationship of abandonment, loss, and suicide (48) has perhaps the most meaning and has stood the test of time.

Life and growth inevitably mean emotional separation from parents. For suicidal youngsters, separation, loss, and death are often equated, are intolerable, and leave the youngsters feeling desperately out of control of their lives. Suicide can be used to control others or to maintain the sense of control over one's own life. To obtain such control, seriously suicidal youngsters often make their living conditional ("I won't live unless I can get into this particular school," "... unless this person will care for me," etc.) (56).

THERAPEUTIC CONSIDERATIONS

The need to use one's death to express desperation, rage, or guilt reflects, among other things, difficulty in using less extreme forms of communication. Understanding and conveying to the patient what it is that he or she is hoping to communicate by dying can provide crucial relief to the patient and can reduce the short-term risk of suicide.

The affective states and their accompanying death fantasies are often activated by trauma and seem, in part, to be an attempt to resolve a dysphoric state through use of a fantasied or dysfunctional object tie.

The patient's own unique psychodynamic constellation of affect, cognition, and meaning is most dramatically prominent immediately before or after a suicide attempt, during what is referred to as a suicidal crisis or episode (14, 57, 58). The same combination of psychodynamic factors is present in suicidal patients during the chronic phases of their illness and is a central element of the individual's psychic life. For example, grandiose fantasies revolving around conquering or controlling death, immortality, or identification with Christ, Hitler, or a UN dignitary are common among suicidal patients. Kohut (59, 60), Kernberg (61), and others have emphasized that such grandiosity usually reflects disturbances in self-esteem and identity formation that occurred early in childhood. The fears of disintegration or identity diffusion that often derive from such developmental disturbances are frequent in borderline or schizophrenic patients who become suicidal, in suicidal veterans with PTSD, and in enraged suicidal patients regardless of their diagnoses. Although the acute threat of disintegration remits as the suicidal crisis is resolved, the underlying identity problems remain, as does the fantasy of resolving them through suicide.

Suicidal patients are unique in their use of the possibility of ending their lives as a way of dealing with both internal conflict and relations with other people. Their use of this possibility colors the transference and countertransference and presents special problems in treatment.

Studies of therapeutic interactions with patients who have killed themselves while in treatment have found that rejection by the therapist was a precipitating factor in many of these cases. Such rejection most often results from the therapist's countertransference anger or hatred, which is often unconscious and often a response to the patient's angry criticisms or demands (62, 63). The patient's threat of dying if his or her demands are not met may lead the therapist to bury awareness of his or her own anger, to feel coerced into obeying such demands, or, conversely, to react punitively to them. Maltzberger and Buie (64) pointed out that the most vulnerable therapists are those whose need to see themselves as able to save any patient renders the possible suicide of a patient narcissistically devastating. Suicidal patients understand the fear they can produce through their death threats and use it in ways that often lead to temporary control over, but eventual rejection by, their therapists as well as others.

Since suicidal patients use their possible death as a way of relating to and controlling the therapist and other people, the psychodynamics underlying their suicidal feelings can be seen in the transference. One young woman, seen following a serious suicide attempt, had persuaded her therapist to call her every morning at 7:00 a.m., threatening that otherwise she would kill herself. Her therapist's anxiety had led him to permit her to act out her fantasy of exercising power over him and over life and death in this manner. Nonetheless, his calling did not prevent an almost fatal suicide attempt.

Early recognition of the role in which the patient is attempting to cast the therapist is critical for progress

in treatment. A young man who survived shooting himself in the chest came into therapy saying he would give the therapist 6 months to make him feel better or else he would be dead. The first months of treatment were spent understanding his need to establish a relationship that made the therapist responsible for whether he lived or died (65).

Therapists may be cast in, or may be tempted to play, the role of saviors. Just as often they are cast in the role of executioners (54). They may be incorporated into patients' rebirth or reunion fantasies, and they often become the targets of suicides motivated by revenge. The therapist of the patient who jumped in front of a train, mentioned earlier, had tried to be available to her in ways that her father was not. Afterward, he realized that she had been determined to perceive him as responsible for her death. Immediately before her attempt and afterward, she made an effort to see to it that the therapist would be blamed. By splitting her feelings toward her father, she could perceive her therapist as the destroying father, making it easier to preserve her fantasy of salvation through reunion with her natural father, whom she could idealize as loving.

EARLY EXPERIENCES

Recent work has questioned the observation by Zilboorg (66) a half-century ago that the loss through death of a parent during the patient's childhood was a significant factor in suicide. Barraclough (67) found that loss of a parent in childhood was no more frequent in his sample of subjects who had committed suicide than it was in his control group. He did find, however, that the recent death of a parent or spouse had occurred significantly more frequently among the subjects who committed suicide.

In adolescents the factors of parental death and recent object loss tend to merge, since a parent's death is likely to have been a recent event. In any case, what Zilboorg was observing was the impact of such deaths on his patients, an impact he attributed to the patient's identification with a dead parent. It is possible that for suicidal patients, even if the frequency of parental death is not extraordinary, its impact is greater, perhaps because of such identification.

More recent study of the families of young people who have killed themselves has indicated that suicide or attempted suicide is disproportionately frequent among the first- or second-degree relatives of these youngsters (68). Whether the factor responsible in these cases is genetic or psychosocial is not clear, and the psychological impact of second-degree relatives' suicide or attempted suicide on young people who eventually kill themselves has not been studied.

Maltzberger and Buie have provided us with a broader explanation of the suicidal patient's vulnerability to loss (69). They build on Kohut's postulate that the experience of an empathic, nurturing mother is a prerequisite for the individual's developing soothing intro-

jects and the ability to comfort himself in times of loss (59, 60). Individuals who lack this ability tend to form relationships in which the other person is not viewed independently but is seen instead as an extension of the self. When these patients experience object loss, they feel a narcissistic insult that can lead to depression or anxiety about disintegration, anxiety that Kohut felt "is the deepest anxiety man can experience" (70). Some patients can turn to other people for comfort, but Maltzberger and Buie point out that suicidal patients have difficulty in doing just this. Instead, they are isolated in a paralyzing sense of aloneness—"a state of vacant cold isolation accompanied by varying degrees of terror"—which these authors liken to the infant's experience of separation anxiety (69).

Object relations theory gives a developmental explanation for the self-punitive elements of suicide. Early intrapsychic conflicts are seen as producing a susceptibility to splitting in the patient's self-representation in times of stress. The suicide may then involve the patient's identifying with the good self and punishing the bad self (50).

The question remains as to why some individuals feel that death is the only way to control their sense of fragmentation or express their need for punishment. Studies of the family relationships of suicidal youngsters may provide some clarification. Retrospective studies conducted in the 1960s and 1970s consistently found that suicidal youngsters were alienated from their families in early childhood by parental attitudes of resentment, hostility, and rejection (55, 71–76). A more recent psychological autopsy study of young suicides confirmed that significantly more frequent parental abuse or rejection had been experienced by the suicidal youngsters than by the control group (77).

Whether these parental responses are reactions to the children's behavior or purely the product of the parents' pathology, the recollections of suicidal youngsters repeatedly invoke parental figures who are frustrating, rejecting, or controlling. Some young people may express their distress through such reckless behavior with cars, motorcycles, or drugs that their parents are forced to acknowledge their self-destructiveness. In some cases the child creates such a disturbance in the family that the parents indicate they wish the youngster were out of the family (75).

In other families the parents seem to want the child's presence, but they do not want to be emotionally involved with the child (16, 55, 76). They want the child to be there and not be there at the same time—to be under their control and to gratify their demands, but not to have any independent character or wishes. The youngster may incorporate parental expectations in a mechanical manner but derives little pleasure or satisfaction from fulfilling them. At the same time, these youngsters do not feel free to act in ways that would separate them from their parents. They often make no emotional demands but instead become withdrawn, depressed, and quietly preoccupied with death and suicide (16, 55, 76).

This formulation is confirmed by an English study of adolescents who were treated psychoanalytically after serious suicide attempts (78). It found that the suicide attempts were triggered by the adolescents' "experience of failure in the attempt to separate from the mother." The failure, which was the outgrowth of a long-standing disturbed parent-child relationship, led to an intensification of maternal ties and to displacement of the experience of rejection and anger from the mother to an external object. Displacement of anger away from the mother diminished the guilt that inhibited action, permitting the anger to be expressed in suicide.

Reconstructions of early family experiences of adults have severe limitations, and most of the retrospective studies of the families of suicidal youngsters have not been controlled studies. Retrospective accounts cannot tell us whether family pathology produced the vulnerability to suicide or whether the family problems developed in response to an already disturbed child. Although the opportunity to observe the families of young patients directly may strengthen the validity of family formulations, the patients' own response to separation may also have biological or genetic roots.

FUTURE DIRECTIONS FOR RESEARCH AND TREATMENT

There is much that we do not know. Recent work on the relation of panic disorder and anxiety to attempted suicide and suicide is likely to focus our attention on the role of anxiety as an important affect in suicidal patients regardless of their diagnosis (5, 33). Evidence suggests that the level of anxiety may distinguish borderline (79) and schizophrenic (9, 10) patients who are suicidal from those who are not. As indicated earlier, there is now more definitive evidence that this is true for patients with major depressive disorders (33).

The capacity to bear hopelessness, rage, anxiety, and other unpleasant affects without collapse or regression (80, 81) has attracted little attention from either biological or psychodynamic investigators. This should change. The capacity or incapacity to self-regulate mood states may derive from biogenetic endowment as well as from struggles over the introjection of ameliorative or destructive objects.

Although suicide often appears to be a form of affect regulation in individuals who feel that their lives are out of control, in some cases the dysregulation and the suicide attempt appear to be expressed in an impulsivity akin to that seen in violent behavior (82, 83). The possibility of measuring the use of particular defense mechanisms to differentiate the relative risks of suicidal and violent behavior is attracting investigators. Pfeffer et al. (84) found that introjection and splitting were fundamental defenses in suicidal children, while compensation, projection, and displacement were correlated with assaultive behavior. Apter et al. (85) found that repression was correlated with risk of suicide, and projection and denial were correlated with risk of vio-

lence, while denial was negatively correlated with risk of suicide. It will be interesting to see what patterns of defense mechanisms emerge in patients who are both suicidal and violent.

In the past decade, specific psychodynamic conflicts seen in suicidal patients have begun to be linked to particular diagnoses. In addition to the rage toward lost love objects that is observed in patients with depression, other such linkages are conflicts over separation and abandonment in persons with borderline personalities (79), fear of disintegration in schizophrenic patients (9, 10), guilt about combat actions in veterans with PTSD (24), and grief over recent loss in alcoholics (20). It would not be surprising if further evidence of such linkages were found.

An understanding of what is known of the psychodynamics of suicide is valuable and critical in treating suicidal patients. There has long been concern about suicidal patients who do not receive appropriate psychotropic medication or are not hospitalized when necessary. Today an equally common concern involves suicidal patients, in or out of hospitals, who are receiving appropriate medication but inadequate psychotherapy. The hoary example of the patient who kills himself after his depression has lifted in response to medication serves as a reminder that more than depression is involved in suicide. The best treatment currently available comes from understanding the interactive role that diagnosis, medication, and psychotherapy play in the treatment of suicidal patients (86). If the psychotherapy of such patients is to be effective, it must be guided by a knowledge of the psychodynamics of suicide.

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Psychosis and Physical Aggression in Probable Alzheimer's Disease

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***Objective:** The purpose of this study was to determine the frequency and type of psychotic symptoms in patients with probable Alzheimer's disease and to test whether there is a relationship between specific psychotic symptoms and episodes of physical aggression. **Method:** From 209 patients with possible or probable Alzheimer's disease who had been assessed in a research clinic every 6 months for up to 4.5 years, 181 subjects with probable Alzheimer's disease were selected for study. On the basis of the summary note for each visit in the patients' charts, the presence of delusions, hallucinations, misidentifications, and episodes of physical aggression was determined. Data regarding psychotic symptoms and aggression were available for 170 and 169 subjects, respectively. **Results:** Delusions had been reported for 74 (43.5%) of the patients and were the most frequent psychotic symptom; persecutory delusions were the most common type. Physical aggression had been noted for 50 (29.6%) of the patients. Delusions and misidentifications frequently preceded and were significantly associated with episodes of physical aggression. The presence of delusions was a significant predictor of physical aggression but accounted for only 3.5% of the variance. **Conclusions:** This study suggests that delusions are a risk factor for physical aggression in patients with probable Alzheimer's disease who have moderate to severe cognitive impairment. As delusions accounted for only a small percentage of the variance, further research is needed to identify other variables that may be significant predictors of physical aggression in this population.*

(Am J Psychiatry 1991; 148:1159-1163)

Alzheimer (1) described delusions, hallucinations, and other behavioral changes in his first case of the disease that bears his name. Delusions and hallucinations in patients with dementia of the Alzheimer type are common (2, 3), cause distress to caregivers (4), and may be amenable to treatment (5). Psychotic

symptoms were associated with extrapyramidal signs (6), poorer cognitive performance (7), and more rapid cognitive decline (7, 8) in some studies but not in others (9, 10).

In addition to delusions and hallucinations, patients with dementia of the Alzheimer type display a variety of abnormal behaviors, such as aggressive outbursts. Physical violence and hitting are reported as serious problems by family caregivers (4), may lead to institutionalization (11), and occur regularly in nursing homes (12). Furthermore, aggressive patients with dementia may be abused by caregivers in response to their own aggression (13). Physical aggression by one nursing home resident with dementia of the Alzheimer type resulted in the death of another resident (14).

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Supported in part by grants AG-05146 and AG-00149 from the National Institute on Aging.

The authors thank Kathryn Carson, B.A., for statistical assistance.
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In a community sample of 183 demented subjects studied by questionnaire (13), the prevalence of physically aggressive behavior (occurring at any time during the dementing illness) reported by caregivers was 46%. Similarly, the frequency of physical aggression in 55 demented subjects seen at a university hospital department of psychiatry was 47% (4). The frequency of assaultive/violent behavior in 126 subjects from a dementia research clinic in a department of neurology was 21% (15), and there was no difference in frequency when specific type of dementia was considered. We are aware of only one study of aggressive acts (both verbal and physical) in subjects with probable Alzheimer's disease (16), and the frequency in that study was 25%. These differences likely reflect varying definitions of aggression, as well as different sources of subjects.

To our knowledge, the relationship between psychotic symptoms and behavior has been studied in only one group of patients with probable Alzheimer's disease (16). In this cross-sectional study, no association between psychotic symptoms and aggressive acts was found. In a heterogeneous group of demented subjects, Swearer et al. (15) found no correlation between the severity of hallucinations or delusions and assaultive behavior. In another investigation (17), newly admitted nursing home patients with delusions were more behaviorally impaired before and after admission than nursing home patients without delusions.

The present investigation was conducted to address the following questions: 1) What are the frequencies and types of delusions, hallucinations, and misidentifications in subjects with probable Alzheimer's disease? and 2) Is there an association between delusions, hallucinations, or misidentifications and at least one episode of physical aggression?

METHOD

In the Alzheimer's Disease Research Center at Johns Hopkins University, 209 subjects with probable or possible Alzheimer's disease are being assessed every 6 months. For this study we reviewed the research clinic charts of 181 enrolled patients with probable Alzheimer's disease. Fifty-six (30.9%) of the subjects had been followed 3.0 to 4.5 years, 61 (33.7%) had been followed 2.0 to 2.5 years, 40 (22.1%) had been followed 1.0 to 1.5 years, nine (5.0%) had been followed for 6 months, and 15 (8.3%) had been seen for one visit. The diagnosis of probable Alzheimer's disease was based on 1) the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) (18) and 2) a score of 6 or less on the Hachinski scale (19). No subject had a current diagnosis of alcohol abuse, schizophrenia, mental retardation, or gross cerebrovascular disease. Of the 181 patients whose charts were reviewed, 112 (61.9%) were recruited from the Dementia Research Clinic at Johns Hopkins Hospital, 34 (18.8%) from primary care physicians in response to a letter announcing our study, 28 (15.5%) from the cognitive neurology department at the Johns Hopkins Hospital, and seven (3.9%) from other sources. The majority of the subjects lived in the Baltimore area.

TABLE 1. Demographic Characteristics of 170 Patients With Probable Alzheimer's Disease

Characteristic	Mean	SD	N	%
Age at onset (years)	65.8	8.3		
Education (years)	12.6	3.7		
Female			111	65.3
White			146	85.9
Marital status at visit 1				
Married			106	62.4
Widowed			46	27.1
Divorced/single			18	9.4
Mini-Mental State score				
at visit 1	14.3	5.6		
Years ill at visit 1	4.0	2.4		

Data regarding psychotic symptoms and physical aggression were available for 170 and 169 subjects, respectively. Demographic characteristics of the 170 patients are presented in table 1.

Evaluations during visit 1 were performed by a research psychiatrist (B.W.R.) and included a modified version of the Present State Examination (20) to elicit psychiatric symptoms. Each subsequent visit was conducted by a research psychiatric nurse (C.S.) and comprised a 30-minute examination of the patient consisting of open-ended questions to elicit psychiatric symptoms and a 30-minute interview with the primary caregiver to complete the Psychogeriatric Dependency Rating Scales (21) and the Scale of Psychosis in Alzheimer's Disease (22). Interrater reliability for these raters has been established. Cognitive state was assessed with the Mini-Mental State examination (23) at each visit. All symptoms were described in the summary note for each visit.

For the current study, the summary notes for all visits were reviewed to determine the presence of psychotic symptoms and episodes of physical aggression. Delusions were rated as present if the descriptions in the summary notes were consistent with the *DSM-III-R* definition and if they occurred more than one time during the preceding 6 months or were reported on two successive clinic visits.

Hallucinations were rated as present if the summary note descriptions were consistent with the *DSM-III-R* definition. Descriptions included details of actual observations of the patient's interaction with internal stimuli during the examination or reports by the caregiver of visual images or of the patient's conversations or physical interaction with such images when no stimulus was present.

Misidentifications, false statements often made by patients with Alzheimer's disease, are thought to be related to visuospatial impairment and reflect the presence of agnosia. This syndrome in Alzheimer's disease

patients is distinct from Capgras' syndrome, in which recognition is intact but the patient has the false belief that an individual has been replaced by an impostor. For this study, a delusional elaboration of a misidentification was considered a delusion if it met the *DSM-III-R* criteria. Misidentification was defined as any of the following: inability to recognize one's self in the mirror and believing that one's reflection is someone else; believing that strangers are living in the house; believing that one's caregiver is someone else; or believing that one needs to "go home" despite the fact that one is home. Illusions, defined as misperceptions of real external stimuli, were also classified as a type of misidentification because they represent false beliefs that appear to be related to defects in sensory processing. Although illusions are not reported frequently, other studies of psychotic symptoms in Alzheimer's disease (7) have included illusions as a type of psychotic symptom.

An episode of physical aggression was defined as the subject's making physical contact with another person or object in an aggressive fashion (e.g., biting, throwing an object, slapping). Threatening behavior, such as raising a hand as if to hit, was not considered an act of physical aggression.

Onset of the dementing illness was determined at the initial visit to the clinic and was defined as the date of the earliest symptom. Age at onset was based on this date. For any chart lacking a specific month of onset, the 6th month of the year was arbitrarily chosen for this study. Latency of a psychotic symptom was determined by calculating the time in months from the onset of the dementing illness until the date of the clinic visit at which the symptom was first reported. If the summary note specified an onset of the symptom before the preceding 6 months, the specified date was used to determine latency. At the time the symptom was first reported, 49.2% of the subjects with delusions (32 of 65), 37.8% of those with hallucinations (14 of 37), and 22.9% of those with misidentifications (11 of 48) were receiving neuroleptics.

RESULTS

The frequencies and types of delusions, hallucinations, and misidentifications are shown in table 2. During the study period, the reports indicated that 43.5% of the subjects had delusions, 30.0% had misidentifications, and 23.5% had hallucinations. According to chi-square analysis with Yates correction, delusions were associated with both hallucinations ($\chi^2=16.4$, $df=1$, $p<0.001$) and misidentifications ($\chi^2=12.1$, $df=1$, $p<0.001$). Of the 74 subjects with delusions, 29 also had hallucinations and 33 had misidentifications. Misidentifications were significantly associated with hallucinations ($\chi^2=14.1$, $df=1$, $p<0.001$); 22 (43.1%) of the 51 subjects with misidentifications also had hallucinations sometime during the course of their illnesses.

TABLE 2. Prevalence and Type of Psychotic Symptoms in 170 Patients With Probable Alzheimer's Disease

Symptom	N	% ^a
Delusions	74	43.5
Persecutory	54	73.0
Reference	11	14.9
Jealousy	7	9.5
Grandiose	1	1.4
Somatic	1	1.4
Thought control	0	0.0
Erotomania	0	0.0
Other	21	28.4
Misidentifications	51	30.0
House is not patient's home	26	51.0
Strangers are living in the house	15	29.4
Own reflection is someone else	11	21.6
Illusion	4	7.8
Caregiver is an impostor	1	2.0
Hallucinations	40	23.5
Visual	34	85.0
Auditory	18	45.0
Tactile	1	2.5
Gustatory	0	0.0
Olfactory	0	0.0

^aPercentages for major subtypes of psychotic symptoms based on total number of subjects. Percentages for specific symptoms based on number of subjects with delusions, misidentifications, and hallucinations, respectively.

The mean \pm SD Mini-Mental State score at the visit at which delusions were reported was 11.9 ± 6.7 ($N=67$), 10.1 ± 7.5 ($N=36$) at the visit at which hallucinations were reported, and 9.3 ± 6.2 ($N=47$) at the time misidentifications were reported. There were no significant differences between the subjects with and without delusions in marital status, gender, age at onset, or educational level. A significantly larger proportion of black subjects (66.7%, $N=16$) than white subjects (39.7%, $N=58$) had delusions (chi-square analysis with Yates correction: $\chi^2=5.04$, $df=1$, $p<0.03$). However, this may not reflect a true racial difference because only a small proportion of the subjects were black ($N=24$).

Persecutory delusions were most often cited and were reported for 31.8% of the patients. One patient believed that four boys were hanging around the house and occasionally hitting her and disrupting her household, and another believed that day care staff were trying to kill him. The second largest category of delusions was the "other" category. Included in this category were such delusions as the belief that people (hallucinated by the patient) in the house were conducting drug sales and the belief of one man that he was in his early 70s, when in fact he was 82, associated with assertions that he must go to the Bureau of Vital Statistics to change his age. Delusions of reference constituted 14.9% of the reported delusions and were usually associated with the misidentification of television characters. Of all the hallucinations reported, 85.0% were visual, and auditory hallucinations were the next most common type. The three most common misidentifications were the patient's belief that he or she was

TABLE 3. Demographic Characteristics of 169 Physically Aggressive and Nonaggressive Patients With Probable Alzheimer's Disease

Characteristic	Aggressive (N=50)				Nonaggressive (N=119)			
	Mean	SD	N	%	Mean	SD	N	%
Age at onset (years)	64.2	8.6			66.3	8.0		
Education (years)	12.5	4.0			12.6	3.5		
Female			33	66.0			77	64.7
White			42	84.0			104	87.4
Marital status at visit 1								
Married			32	64.0			74	62.2
Widowed			13	26.0			32	26.9
Divorced/single			5	10.0			13	10.9

not home, the belief that strangers were living in the house, and misidentification of the patient's own reflection in the mirror.

Fifty patients (29.6%) were reported by their caregivers to have been physically aggressive at least one time during the course of the illness. Many episodes could be categorized as situational, for instance, when the caregiver was attempting to help the patient during grooming or stopped the patient during attempts "to go home." The remainder appeared to be spontaneous and unrelated to a specific caregiving activity. Of the 50 physically aggressive episodes reported for this group, 23 (46.0%) were situational and 27 (54.0%) were nonsituational. Many of the patients with spontaneous aggression used weapons (e.g., chair, scissors, or knife). In addition, two patients in this group were described as self-mutilating; one subject pinched and scratched herself and pulled her own hair, and the other bit himself. The physically aggressive subjects were not different from the nonaggressive subjects in demographic characteristics (table 3) or past history of depression or alcohol abuse. The majority of aggressive episodes (68.0%) occurred while the patients were living at home.

A primary focus of this investigation was the relationship between psychotic symptoms and episodes of physical aggression (see table 4). Delusions (N=27) and misidentifications (N=19) were reported before or at the same visit as an aggressive episode in 90.0% and 90.5% of the cases, respectively. Similarly, of the 17 aggressive patients with hallucinations, hallucinations were reported before or at the same visit as the physical aggression for 88.2%. To examine this relationship further, chi-square analyses were performed. The prevalences of delusions and misidentifications were significantly higher in the physically aggressive group. The prevalence of hallucinations was also higher in the aggressive group and approached significance. In addition, stepwise binary multiple regression was performed to examine which symptom most strongly predicted an episode of physical aggression. Delusions were the best predictor of physical aggression, although the percentage of variance explained was low

TABLE 4. Prevalence of Psychotic Symptoms in 169 Physically Aggressive and Nonaggressive Patients With Probable Alzheimer's Disease^a

Type of Psychotic Symptom	Aggressive (N=50)		Nonaggressive (N=119)	
	N	%	N	%
Delusions	30	60.0	44	37.0
Misidentifications	21	42.0	29	24.4
Hallucinations	17	34.0	23	19.3

^aAccording to chi-square analysis with Yates correction, difference between groups was significant for delusions ($\chi^2=6.68$, $df=1$, $p<0.01$) and misidentifications ($\chi^2=4.44$, $df=1$, $p<0.05$) and nearly significant for hallucinations ($\chi^2=3.42$, $df=1$, $p<0.06$).

($R^2=0.0348$, $F=5.9$, $df=1$, 164 , $p=0.02$). In the presence of delusions, neither misidentifications (change in $R^2=0.0125$, $F=2.13$, $df=2$, 163 , $p>0.14$) nor hallucinations (change in $R^2=0.0034$, $F=0.58$, $df=3$, 162 , $p>0.44$) explained a significant additional amount of variance.

DISCUSSION

The major finding of the study is the association of delusions and misidentifications with at least one episode of physical aggression. The longitudinal design of our study and the narrow definition of physical aggression differ from those in the study reported by Mendez et al. (16) and may account for the difference in findings. Our study suggests that delusions are a risk factor for an episode of physical aggression in patients with probable Alzheimer's disease.

In this cohort, persecutory delusions were the most common psychotic symptom reported by caregivers. Specifically, themes of suspiciousness, stealing, and threats of bodily harm were most commonly reported. In contrast to the symptoms of schizophrenia and major affective disorder, delusions of thought control and somatic, nihilistic, and grandiose delusions were rarely reported in this group. These findings are similar to those previously reported (3, 16). Moreover, many of the patients for whom hallucinations and misidentifications were reported also experienced delusions at some time during the course of illness. By contrast, many of the patients with delusions did not experience hallucinations or misidentifications.

The generalizability of these results may be limited by a bias of ascertainment. Our findings may overestimate the frequency of psychiatric symptoms in patients with probable Alzheimer's disease because the majority of our subjects were recruited from a department of psychiatry. On the other hand, since 50.0% of the nondelusional subjects received neuroleptics for other behavioral symptoms, the expression of delusions may have been obscured in these subjects, contributing to an underestimation of frequency. However, the frequencies reported here are similar to those reported from an Alzheimer's disease clinic within a

department of neurology (16). Our study group consisted of subjects whose level of cognitive impairment was moderate to severe. Therefore, these findings may not be generalized to subjects with early Alzheimer's disease who have Mini-Mental State scores higher than 20.

One limitation of this type of study is the lack of reliable and valid rating scales with which to assess the presence and severity of these symptoms in patients with dementia (24). We relied on a detailed clinical interview with both the patient and primary caregiver that focused on the presence of specific psychiatric and behavior problems. The method of assessment of aggressive episodes differentiated caregiver report of physical aggression from verbal aggression and a variety of other behavioral problems.

The results of this study are important because delusions are common in patients with probable Alzheimer's disease, are associated with physical aggression, and are potentially treatable. A single-blind pilot study of haloperidol for the treatment of psychosis in probable Alzheimer's disease (5) revealed a significant decrease in the Brief Psychiatric Rating Scale (25) psychosis factor. However, substantial extrapyramidal signs and cognitive deterioration occurred. To our knowledge, a double-blind placebo-controlled trial of neuroleptic treatment of delusions in patients with probable Alzheimer's disease has not been completed, and the determination of the best dose for demented patients must also be carefully examined.

An important finding of this study was that a substantial proportion of the episodes of physical aggression occurred during caregivers' interactions with delusional patients. This is similar to the finding that verbal aggression commonly occurs in situations where the patient is being directed by the caregiver (26). Moreover, this latter study demonstrated that the premorbid social relationship between patient and caregiver is one predictor of aggression in demented patients. Although our data do not yield information confirming or refuting this contention, the style of interaction may play a role in precipitating an aggressive response.

Further research is needed to identify other variables, such as level of cognitive impairment, functional ability, premorbid behavioral problems, and caregiver characteristics, that may be predictors of physical aggression in patients with clinical Alzheimer's disease.

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The Influence of Major Depression on Clinical and Psychometric Assessment of Senile Dementia of the Alzheimer Type

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Objective: The performance on standard clinical and psychometric assessments of eight elderly individuals with major unipolar depression alone and seven with depression plus mild senile dementia of the Alzheimer type was compared with that of 41 nondepressed subjects suffering from very mild senile dementia of the Alzheimer type, 66 with mild senile dementia of the Alzheimer type, and 83 age-matched subjects without senile dementia. **Method:** Subjects with depression alone, depression plus mild senile dementia of the Alzheimer type, and very mild and mild senile dementia of the Alzheimer type met strict inclusionary and exclusionary criteria. A 90-minute semistructured interview, including several brief standardized clinical scales, was used to assign a Clinical Dementia Rating to each subject according to published guidelines, and each subject was given a 2-hour psychometric test battery. Data were analyzed by one-way multivariate analysis of variance to ascertain if there was an effect of group on clinical and psychometric test scores. **Results:** The eight depressed subjects without concurrent dementia performed as well as the 83 nondepressed subjects without dementia on most clinical measures; however, their performance on most psychometric measures closely resembled that of the 41 nondepressed subjects with very mild dementia. The performance of the seven subjects with depression plus mild dementia was comparable to that of the 66 nondepressed subjects with mild dementia on most clinical and psychometric measures. **Conclusions:** Although depressed subjects performed as well as subjects without dementia on many clinical assessments, psychometric testing was not able to distinguish depressed subjects from those with very mild senile dementia of the Alzheimer type. This demonstrates the need for careful psychiatric evaluation before interpreting deficits on psychometric tests as indicating the presence of very mild senile dementia of the Alzheimer type.

(Am J Psychiatry 1991; 148:1164-1171)

In otherwise healthy subjects, the clinical diagnosis of senile dementia of the Alzheimer type by experienced physicians using standardized criteria can be highly accurate (1-3). The Washington University Clinical Dementia Rating categorizes the severity of dementia as questionable or very mild, mild, moderate, and severe (ratings of 0.5, 1, 2, and 3, respectively) (2, 4, 5). In

subjects with senile dementia of the Alzheimer type without complicating medical, neurological, or psychiatric illnesses, this scale has proven reliable (6). In addition, the validity of this scale—that a Clinical Dementia Rating of 1 or greater represents Alzheimer's disease—has been neuropathologically demonstrated (3). (In this paper, the term "Alzheimer's disease" refers to the histologically proven disorder, whereas "senile dementia of the Alzheimer type" refers to the disease diagnosed by clinical and laboratory criteria.) In another study (7) we demonstrated that the majority of subjects with a Clinical Dementia Rating of 0.5 (questionable or very mild dementia) were in fact ill with very mild senile dementia of the Alzheimer type, which progressed to more severe illness.

The Clinical Dementia Rating is based on a 90-minute semistructured interview administered to the subject and a knowledgeable collateral source by an experienced research physician (4, 5). In addition to open-ended questions, every individual is given several

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Supported in part by National Institute on Aging grants AG-05681 and AG-03911 and NIMH grant MH-31054.

The authors thank the entire staff of the Alzheimer's Disease Research Center at Washington University and especially Dr. Leonard Berg for his continued collaboration and critical reading of this paper.

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standard clinical scales as well as a psychometric battery assessing several domains, including memory, speech, visuospatial capabilities, and timed motor performance (8, 9). Our group has published the results of these multiple clinical and psychometric assessments comparing healthy subjects with individuals having very mild, mild, moderate, or severe dementia (1, 2, 4, 5, 7–10).

Major depression in elderly adults is a common, frequently debilitating illness that influences behavior and function. The literature concerning the cognitive deficits produced by depression in elderly adults is sparse (11–15). In addition, major depression can occur in individuals with dementia (14). The purpose of the current study was to examine the effect of geriatric depression on performance on the clinical and psychometric batteries used in our dementia studies.

METHOD

Diagnostic criteria, subject recruitment, and description of the subjects without dementia (Clinical Dementia Rating of 0) and individuals with questionable or very mild (Clinical Dementia Rating of 0.5) and mild (Clinical Dementia Rating of 1) senile dementia of the Alzheimer type are given in detail elsewhere (4, 5, 7). The diagnostic criteria for senile dementia of the Alzheimer type are compatible with those of *DSM-III* and the NINCDS-ADRDA Work Group (16).

The data pertaining to these groups of subjects are from the initial assessments of two longitudinal studies (the first began in 1979 and the second in 1984). In the first longitudinal study, 58 subjects without dementia, 16 subjects with questionable or very mild senile dementia of the Alzheimer type (Clinical Dementia Rating of 0.5), and 44 subjects with mild senile dementia of the Alzheimer type (Clinical Dementia Rating of 1) were enrolled. In the second longitudinal study, 25 subjects without dementia, 25 subjects with questionable or very mild senile dementia of the Alzheimer type, and 24 subjects with mild senile dementia of the Alzheimer type were enrolled. Initial psychometric data were missing for two of the subjects with mild senile dementia of the Alzheimer type; these subjects are not included in the analyses reported here. All subjects met rigorous inclusion and exclusion criteria. Individuals with possible confounding medical, neurological, or psychiatric disorders (including depression) were not enrolled.

For the purpose of the present study, eight elderly adults with major depression but without senile dementia of the Alzheimer type and seven elderly adults with concurrent major depression and mild senile dementia of the Alzheimer type (Clinical Dementia Rating of 1) were enrolled. Other than depression, these individuals met the same criteria as the subjects without dementia and the subjects with mild senile dementia of the Alzheimer type enrolled in the longitudinal studies. Subjects with depression met *DSM-III* and Feighner (17) criteria. In addition to fulfilling these criteria, each case

was reviewed by one of us (E.H.R.), who agreed that clinical depression was present. Each of the subjects with depression only and depression plus mild senile dementia of the Alzheimer type was given the Beck Depression Inventory (18) and the Geriatric Depression Scale of Yesavage et al. (19).

Each subject and a knowledgeable collateral source (usually the spouse or other close relative) were given a semistructured 90-minute interview by a research physician (neurologist, psychiatrist, or geriatrician) (4, 5). This assessment included open-ended questions as well as structured questions that allowed the scoring of several brief clinical scales. These scales included the Dementia Scale of Blessed et al. (20), the cognitive portion of the Dementia Scale (the full scale minus the 11 personality questions) (20), the Short Portable Mental Status Questionnaire (21), and an aphasia battery (22). Participants in the second longitudinal study and the subjects with depression alone and those with depression plus mild senile dementia of the Alzheimer type were also given the Short Blessed Test (23) and the Blessed Information-Memory-Concentration Test (20).

All procedures and methods for obtaining informed consent from subjects and responsible relatives were approved by the Human Studies Committee of Washington University.

Information from the entire clinical assessment was used to rate the subject on six "box scores." Each "box" represented cognitive function in one of the following spheres: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. A composite Clinical Dementia Rating was obtained from the six individual "box scores" by using established guidelines (4). The sum of the six individual box scores is referred to as the "sum of boxes." Answers to open-ended questions in the clinical assessment concerning mental and physical health together with the 11 personality items of the Blessed Dementia Scale were also used to classify personality changes into three groups—passive changes, agitation, and self-centeredness—as previously described (24–26).

A 2-hour psychometric test battery was independently administered by research psychometricians. The results of this battery were not available to the research physicians when the Clinical Dementia Rating was assigned. This battery examines a variety of psychological functions, including verbal and nonverbal functions, primary and secondary memory (e.g., subtests of the Wechsler Memory Scale [27] and the Benton Visual Retention Test [28]), language skills (e.g., the Boston Naming Test [29] and Word Fluency [30]), psychomotor performance (e.g., Trailmaking A [31] and Crossing-Off [32]), visuospatial abilities (e.g., the copying form of the Benton Visual Retention Test [28]), and intelligence (subtests of the Wechsler Adult Intelligence Scale (WAIS) [33]). Discussions of the strengths and limitations of these measures relative to measurement of cognitive abilities in subjects with senile dementia of the Alzheimer type have been published elsewhere (8, 9).

TABLE 1. Age, Education, and Socioeconomic Status of Nondepressed and Depressed Subjects With and Without Senile Dementia of the Alzheimer Type^a

Item	Comparison Subjects (N=83)		Nondepressed Subjects With Dementia				Depressed Subjects			
			Very Mild Dementia (N=41)		Mild Dementia (N=66)		Depression Only (N=8)		Depression Plus Mild Dementia (N=7)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	71.6	4.9	73.9	5.2	72.2	5.0	72.5	4.8	74.6	6.6
Education (years)	13.2	3.3	13.0	3.8	12.1	3.7	11.6	4.7	10.6	3.6
Socioeconomic status	2.9	1.1	3.0	1.1	3.3	1.1	3.2	1.4	3.9	0.7

^aF=1.46, df=15, 524, p=0.14, MANOVA with group as the independent variable and age, education, and socioeconomic status as dependent variables.

The measures of memory in the standard psychometric battery are of immediate, intentional memory. Hart et al. (34) suggested that measurement of incidental recall may be helpful in differentiating depressed subjects from those with mild dementia. Therefore, a test of incidental recall of the symbols from the WAIS digit symbol subtest was given to the subjects with depression only and to subjects in the longitudinal studies during a follow-up visit. The total number of symbols recalled was recorded as well as the number of symbols matching the correct numeral (exact match). This test of incidental memory differed slightly from that reported by Hart et al. in that subjects saw the symbols only for 90 seconds, the standard length of time for the digit symbol task. In the study reported by Hart et al., subjects were allowed to complete the answer sheet without regard to time.

All data reported are from initial assessments, except for the incidental recall tests in subjects without dementia and those with very mild or mild senile dementia of the Alzheimer type, whose assessments were administered during an annual follow-up visit. In the infrequent circumstance where a specific test was not administered, the mean value for the group was used for statistical analysis.

Demographic data, clinical tests (except for the Short Blessed Test and the Blessed Information-Memory-Concentration Test), psychometric tests, and incidental recall tests were each analyzed by one-way multivariate analysis of variance (MANOVA). Post hoc analyses were performed with Ryan-Einot-Gabriel-Welsch multiple F tests for all dependent variables used in the MANOVA. The independent variable for each MANOVA was group (comparison subjects, nondepressed subjects with very mild senile dementia of the Alzheimer type, nondepressed subjects with mild senile dementia of the Alzheimer type, subjects with depression only, and subjects with depression plus mild senile dementia of the Alzheimer type). The dependent variables for the MANOVA involving demographic data included age, number of years of education, and socioeconomic status according to Hollingshead's index of social position (35). The dependent variables for the MANOVA involving clinical tests were the results from the aphasia battery, the Blessed Dementia Scale, the cognitive por-

tion of the Blessed Dementia Scale, the Short Portable Mental Status Questionnaire, and the sum of the box scores from the physician-rated clinical assessment described earlier in this paper. The dependent variables for the MANOVA involving the psychometric test battery were the results of 19 separate tests: logical memory, mental control, and easy, hard, and total associate learning (recall) on the Wechsler Memory Scale; forward, backward, and total on the Digit Span; S, P, and total on the Word Fluency; the Boston Naming Test; forms C and D of the Visual Retention Test; information, block design, and digit symbol tests on the WAIS; the Trailmaking test; and the Crossing-Off test. The dependent variables for the MANOVA involving incidental recall testing were the results of the WAIS digit symbol, the total number of symbols recalled, and the total number of symbols matched to the correct numeral. The results from the two tests administered in the second but not the first longitudinal study (the Short Blessed Test and the Blessed Information-Memory-Concentration Test) were analyzed by analysis of variance (ANOVA).

The general linear model (Proc GLM) in SAS (36) was used for these analyses. Differences in the percentage of patients with personality changes were examined with chi-square analysis followed by two-tailed Fisher's exact tests to determine which groups were significantly different from the comparison subjects. Data for the comparison subjects as well as subjects with questionable or very mild senile dementia of the Alzheimer type and those with mild senile dementia of the Alzheimer type have been published elsewhere (7, 9, 26) but are included for comparison with the data for subjects with depression only and depression plus mild senile dementia of the Alzheimer type.

RESULTS

There were 32 men and 51 women in the group of subjects without dementia (comparison group); 23 men and 18 women in the nondepressed group with very mild senile dementia of the Alzheimer type; 29 men and 37 women in the nondepressed group with mild senile

TABLE 2. Clinical Test Results of Nondepressed and Depressed Subjects With and Without Senile Dementia of the Alzheimer Type

Item	Nondepressed Subjects With Dementia						Depressed Subjects			
	Comparison Subjects (N=83)		Very Mild Dementia (N=41)		Mild Dementia (N=66)		Depression Only (N=8)		Depression Plus Mild Dementia (N=7)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Aphasia battery ^{a,b}	0.17 _a	0.43	1.02 _a	1.45	3.92 _b	4.63	0.66 _a	1.42	2.19 _{a,b}	2.10
Blessed Dementia Scale ^{a,b}	0.36 _a	0.88	2.61 _b	1.92	5.43 _c	2.87	2.95 _b	2.44	10.89 _d	5.70
Blessed Dementia Scale, cognitive portion ^{a,b}	0.14 _a	0.37	1.32 _b	0.90	3.25 _c	1.41	0.25 _a	0.38	5.93 _d	3.18
Short Portable Mental Status Questionnaire (errors) ^{a,b}	0.39 _a	0.62	1.90 _b	1.81	5.70 _c	2.23	0.62 _{a,b}	0.74	5.00 _c	3.00
Sum of boxes ^{a,b}	0.02 _a	0.12	2.13 _b	1.10	6.18 _c	1.36	0.19 _a	0.26	6.29 _c	1.25
Short Blessed Test ^{b,c}	1.60 _a	2.08	8.20 _b	5.50	18.67 _c	5.58	3.00 _a	3.85	15.14 _c	8.05
Blessed Information-Memory-Concentration Test ^{b,d}	1.20 _a	1.22	6.08 _b	4.07	15.42 _c	4.93	2.25 _a	2.38	11.83 _c	7.11

^aF=38.8, df=20, 651, p≤0.0001, MANOVA with group as the independent variable and the first five tests as the dependent variable set.

^bDifferent subscript letters indicate that the groups' mean scores differed statistically on each test; matching subscript letters indicate that the groups' mean scores did not differ significantly: post hoc analysis (Ryan-Einor-Gabriel-Welsch multiple F tests).

^cFor subjects with no dementia, very mild dementia, and mild dementia, N=25, N=25, and N=24, respectively. F=43.0, df=4, 84, p≤0.0001, ANOVA.

^dFor subjects with no dementia, very mild dementia, and mild dementia, N=25, N=25, and N=24, respectively. F=45.5, df=4, 84, p≤0.0001, ANOVA.

TABLE 3. Results of Psychometric Tests for Nondepressed and Depressed Subjects With and Without Senile Dementia of the Alzheimer Type

Psychometric Test	Nondepressed Subjects With Dementia						Depressed Subjects			
	Comparison Subjects (N=83)		Very Mild Dementia (N=41)		Mild Dementia (N=66)		Depression Only (N=8)		Depression Plus Mild Dementia (N=7)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Wechsler Memory Scale										
Logical memory ^a	9.0 _a	2.5	4.7 _b	2.1	1.7 _c	1.8	5.9 _b	2.2	1.4 _c	1.6
Mental control ^a	7.2 _a	1.9	5.6 _{a,b}	2.3	4.5 _b	2.6	5.1 _{a,b}	2.9	4.0 _b	4.1
Associate learning (recall)										
Easy ^a	16.4 _a	1.6	13.5 _b	2.6	10.8 _c	4.2	14.2 _{a,b}	2.9	9.0 _c	3.5
Hard ^a	4.8 _a	2.9	1.5 _{b,c}	2.1	0.3 _c	0.7	3.2 _{a,b}	2.7	0.3 _c	0.4
Total ^a	13.0 _a	3.4	8.2 _b	3.0	5.7 _c	2.4	10.4 _b	4.0	4.7 _c	1.7
Digit Span										
Forward ^a	6.8 _a	1.1	6.2 _{a,b}	1.3	5.8 _{a,b}	1.2	6.6 _{a,b}	1.2	5.7 _b	0.8
Backward ^a	5.2 _a	1.3	4.1 _{a,b}	1.3	3.2 _b	1.4	3.8 _b	1.8	1.4 _c	1.4
Total ^a	12.0 _a	2.2	10.3 _{a,b}	2.4	8.9 _{b,c}	2.2	10.4 _{a,b}	2.9	7.1 _c	2.0
Word Fluency										
S ^a	14.3 _a	5.5	11.5 _a	5.8	6.8 _b	4.8	13.0 _a	8.6	4.4 _b	2.9
P ^a	13.7 _a	5.2	10.6 _a	5.1	6.3 _b	4.2	10.9 _a	5.9	3.6 _b	4.0
Total ^a	27.9 _a	10.0	22.1 _a	10.5	13.1 _b	8.8	23.9 _a	14.2	8.0 _b	6.8
Boston Naming ^a	53.6 _a	5.1	42.5 _b	12.7	28.5 _c	15.9	50.2 _{a,b}	5.9	29.4 _c	13.6
Benton Visual Retention Test										
Form C: 10-second delay (number of errors) ^a	7.1 _a	3.4	11.7 _b	4.1	16.8 _c	5.2	10.9 _b	5.2	19.4 _c	3.9
Form D: copy (number of errors) ^a	0.7 _a	1.3	1.3 _{a,b}	2.3	3.5 _{b,c}	4.1	0.6 _a	0.5	4.0 _c	3.9
WAIS										
Information ^a	20.1 _a	4.6	14.1 _b	5.5	8.8 _c	5.5	14.2 _b	5.6	8.7 _c	5.9
Block design ^a	29.1 _a	7.5	19.3 _{b,c}	10.1	12.5 _{c,d}	11.1	23.0 _{a,b}	11.8	7.4 _d	9.4
Digit symbol ^a	44.9 _a	11.5	31.9 _b	10.4	18.9 _c	12.6	31.8 _b	16.4	7.0 _d	13.4
Trailmaking (seconds) ^a	42.1 _a	12.5	68.2 _a	32.9	104.0 _b	50.0	60.0 _a	26.0	120.0 _b	58.0
Crossing-Off ^a	171 _a	35	145 _{a,b}	46	124 _b	39	125 _b	18	91 _c	34

^aF=6.8, df=68, 724, p≤0.0001, MANOVA using group as the independent variable and the results of all 19 tests in the psychometric battery as the dependent variable set. Different subscript letters indicate that the groups' mean scores differed statistically on each test; matching subscript letters indicate that the groups' mean scores did not differ significantly: post hoc analysis (Ryan-Einor-Gabriel-Welsch multiple F tests).

TABLE 4. Results of Tests of Recall in Nondepressed and Depressed Subjects With and Without Senile Dementia of the Alzheimer Type

Test of Recall	Comparison Subjects (N=26)		Nondepressed Subjects With Dementia				Depressed Subjects Without Dementia (N=8)	
			Very Mild Dementia (N=9)		Mild Dementia (N=12)			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Digit symbol ^{a,b}	44.1 _a	12.0	38.0 _a	11.3	29.9 _a	15.7	31.8 _a	16.4
Incidental recall: total number of symbols recalled ^a	6.8 _a	1.4	5.1 _{a,b}	2.1	0.6 _c	1.2	4.6 _b	3.1
Exact match recall: total number of symbols recalled that correctly matched ^a	5.3 _a	2.4	3.6 _a	2.7	0.2 _b	0.4	3.1 _a	2.8

^aF=8.71, df=9, 119, $p \leq 0.0001$, MANOVA using group as the independent variable and the three tests as the dependent variable set. Different subscript letters indicate that the groups' mean scores differed statistically on each test; matching subscript letters indicate that the groups' mean scores did not differ significantly: post hoc analysis (Ryan-Einot-Gabriel-Welsch multiple F tests).

^bF=3.81, df=3, 51, $p=0.02$, ANOVA.

dementia of the Alzheimer type; one man and seven women in the group with depression only; and three men and four women in the group with depression plus mild senile dementia of the Alzheimer type. The ratios of men to women were not significantly different ($p=0.16$). The mean±SD age, number of years of education, and socioeconomic status (35) of the five groups are presented in table 1. There were no significant differences among the groups in age, education, and socioeconomic status (table 1). The subjects with depression only and those with depression plus mild senile dementia of the Alzheimer type scored in the depressed range on both the Beck Depression Inventory (19.4 ± 6.0 and 14.9 ± 7.3 , respectively) and the Geriatric Depression Scale (20.0 ± 3.7 and 15.7 ± 7.7 , respectively).

The results from the clinical batteries are presented in table 2. The results of the MANOVA were highly significant (table 2). Similarly, ANOVA results were significant for the Short Blessed Test and the Blessed Information-Memory-Concentration Test (table 2). The performance of the subjects with depression only on the clinical measures was not significantly different from that of subjects without dementia, with the exception of the Blessed Dementia Scale. Subjects with depression only resembled those with very mild senile dementia of the Alzheimer type on this measure. The personality portion of the Blessed Dementia Scale was responsible for this difference because the mean score of subjects with depression only did not differ from that of subjects without dementia on the cognitive portion of the Blessed Dementia Scale. The performance of the subjects with depression plus mild senile dementia of the Alzheimer type on these clinical batteries resembled that of the subjects with mild senile dementia of the Alzheimer type on most of the scales. Their performance on the Blessed Dementia Scale was more impaired than that of the subjects with mild senile dementia of the Alzheimer type who were not depressed, however.

MANOVA results for performance on psychometric tests were highly significant (table 3). The psychometric test performance of depressed subjects without dementia resembled that of subjects with very mild dementia

of the Alzheimer type on most tests. Depressed subjects, however, were more comparable to subjects with mild dementia of the Alzheimer type on the Crossing-Off test of speeded psychomotor performance. Subjects with both depression and senile dementia of the Alzheimer type performed at the same level as those with mild senile dementia of the Alzheimer type on most tests. Their poorest performances occurred primarily on visuospatial tasks (block design, digit symbol) and psychomotor tests (Trailmaking and Crossing-Off).

In the incidental recall and exact match recall assessments (table 4), the subjects with depression without dementia performed at the level of subjects with very mild senile dementia of the Alzheimer type and substantially better than those with mild senile dementia. The fact that digit symbol values for the subjects with very mild and mild dementia in table 4 are higher than those in table 3 may be related to a possible bias introduced by using subjects with very mild and mild dementia at annual follow-up visits rather than at the first visit. Individuals who were available for retest 15–34 months after the first visit may have had slightly milder illness. Although post hoc analysis did not differentiate among the four groups (probably because of the small sample sizes and substantial variability), the individual ANOVA for digit symbol performance was statistically significant (table 4).

Personality changes in the subjects with depression only were different from those of subjects without dementia and most closely resembled those of subjects with very mild dementia (table 5). The prevalence of personality changes in the subjects with depression plus mild senile dementia of the Alzheimer type was as high or higher than that previously reported for subjects with mild dementia (26).

DISCUSSION

There are four major conclusions of this study. 1) Major depression in the absence of dementia influences psychometric performance, particularly in areas such as

TABLE 5. Personality Changes in Nondepressed and Depressed Subjects With and Without Senile Dementia of the Alzheimer Type^a

Item	Comparison Subjects (N=83)		Nondepressed Subjects With Dementia				Depressed Subjects			
			Very Mild Dementia (N=41)		Mild Dementia (N=66)		Depression Only (N=8)		Depression Plus Mild Dementia (N=7)	
	N	%	N	%	N	%	N	%	N	%
Passive ^b	0	0	17	41	48	71	4	50	7	100
Agitated ^c	4	5	14	34	21	31	1	13	4	57
Self-centered ^d	4	5	14	34	29	43	4	50	6	86
Passive, agitated, and self-centered ^e	0	0	5	12	9	13	1	13	4	57
Passive, agitated, or self-centered ^f	8	10	27	66	57	84	5	63	7	100

^aAll groups were significantly different from the group with no dementia (two-tailed Fisher's exact test, $p < 0.05$) in each category of personality change with the exception of the group with depression only, which did not differ significantly for agitated behavior and presence of all three personality changes.

^b $\chi^2 = 94.8$, $df = 4$, $p < 0.001$.

^c $\chi^2 = 27.0$, $df = 4$, $p < 0.001$.

^d $\chi^2 = 44.0$, $df = 4$, $p < 0.001$.

^e $\chi^2 = 29.6$, $df = 4$, $p < 0.001$.

^f $\chi^2 = 96.8$, $df = 4$, $p < 0.001$.

visuospatial functioning and timed motor performance, to a greater degree than it influences performance on clinical assessments. 2) Depression plus mild dementia may lead to disproportionately poorer performance on psychometric testing than on clinical scales. 3) Depressed individuals without dementia perform at the same level as do nondepressed individuals with very mild dementia on tests of incidental recall. Subjects with depression only and those with very mild dementia perform better than do subjects with mild dementia. 4) Depressed individuals without dementia and nondepressed individuals with very mild dementia show similar personality changes. These conclusions are based on small groups of subjects with depression alone and depression plus mild senile dementia of the Alzheimer type; therefore, they should be considered somewhat tentative. It is also possible that, in some instances, true group differences existed that were not apparent due to lack of statistical power.

This study involved 15 depressed individuals who were willing to volunteer several hours of their time. Although all of our subjects fulfilled very strict criteria for major depression, it is likely that many patients with severe depression (such as those with severe melancholia or marked psychomotor retardation) would be less willing to volunteer for such studies. Although we cannot assess the effect of such selection biases, it is likely that melancholic, depressed patients would perform as poorly as or worse than our volunteer depressed subjects. All but one of our depressed subjects without dementia were women. Although we are unaware of data suggesting an effect of gender on performance of elderly depressed individuals on the assessments used in this study, this should probably be examined in future work.

This study was designed to determine whether individuals suffering from depression could be differentiated from those suffering from very mild or mild senile

dementia of the Alzheimer type by using standard clinical and psychometric tests already used in the diagnosis of dementia. Our results indicate that patients suffering from depression without evidence of dementia demonstrate global psychometric impairment involving memory, speech, visuospatial abilities, and motor performance that are quantitatively similar to impairments found in people with very mild dementia (Clinical Dementia Rating of 0.5). Similarities in amounts or types of deficits do not imply similarities in pathophysiology. Considerable research has been devoted to the nature of cognitive deficits associated with depression. Weingartner et al. (37) have postulated that depression differentially affects cognitive processes requiring effort and motivation. Whether elderly individuals are more susceptible to the cognitive deficits associated with depression is a subject of some debate (13).

Hart et al. (34) suggested that tests of incidental recall may differentiate individuals with depression from those with dementia. Our results concur in that the eight depressed subjects without dementia performed much better than 12 of the nondepressed subjects with mild dementia (table 4). However, we could not differentiate the performance on tests of incidental recall of the depressed subjects from that of nine of the subjects with very mild senile dementia of the Alzheimer type. Our previous longitudinal studies have documented that the majority of subjects with very mild senile dementia of the Alzheimer type have a progressive dementing illness. Thus, measures of both intentional and incidental recall may be useful in differentiating patients with depression from those with mild dementia, but neither type of recall differentiates patients with depression from those with very mild dementia.

In contrast to the results of Hart et al. (34), the eight depressed subjects without dementia in our study did not do as well as 26 of the nondepressed subjects without dementia on total incidental recall: in our study the

scores were 4.6 (depression only) and 6.8 (no dementia or depression); in that of Hart et al. they were 6.1 (depression) and 6.9 (no dementia or depression). However, the number of symbols correctly matched with the appropriate numeral by our depressed subjects was not statistically different from that of subjects without dementia: in our study the scores were 3.1 (depression only) and 5.3 (no dementia or depression); in that of Hart et al. they were 4.3 (depression) and 6.4 (no dementia or depression). The reason for this discrepancy is unclear. One possibility is the fact that subjects in our study viewed the symbols for 90 seconds, the standard time for the digit symbol task, but in the study reported by Hart et al. subjects were allowed to see the symbols for as long as they needed to complete the task. We examined the possible effect of this difference by residualizing the recall measures with respect to the number of digit symbol pairs completed in the digit symbol test in an analysis of partial variance (38). The results did not support the conclusion that this methodological difference was responsible for the differences in results.

This study verifies the need to couple clinical history and differential diagnosis with psychometric performance results. As objective psychometric and clinical scales become more commonly used in geriatrics, it is essential to realize that compromised performance on psychometric batteries may reflect illnesses other than dementia. Further careful interdisciplinary studies should allow elucidation of the mechanisms responsible for impaired intellectual performances in these various disorders.

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New Policy for References

Effective with the September 1991 issue, *The American Journal of Psychiatry* will institute a policy of listing the names of all authors of work cited in references. Authors of submitted manuscripts and letters to the Editor must include the surnames and initials of all authors in references. The use of "et al." is no longer acceptable.

Are Depressive Symptoms Nonspecific in Patients With Acute Stroke?

J. Paul Fedoroff, M.D., Sergio E. Starkstein, M.D.,
Rajesh M. Parikh, M.D., Thomas R. Price, M.D., and Robert G. Robinson, M.D.

Objective: Some investigators have suggested that major depression might be overdiagnosed in stroke patients because of changes in appetite, sleep, or sexual interest caused by their medical illness; others have suggested that depression may be underdiagnosed in stroke patients who deny symptoms of depression because of anosognosia, neglect, or aprosody. The authors' goal was to determine how frequently depressive symptoms occur in acute stroke patients with and without depressed mood to estimate how often diagnostic errors of inclusion or exclusion may be made. **Method:** They examined the rate of autonomic and psychological symptoms of depression in 205 patients who were consecutively hospitalized for acute stroke. Eighty-five (41%) of these patients had depressed mood, and 120 (59%) had no mood disturbance. Forty-six (54%) of the 85 patients with depressed mood (22% of all patients) were assigned the DSM-III diagnosis of major depression. **Results:** The 120 patients without mood disturbance had a mean of one autonomic symptom, but the 85 patients with depressed mood had a mean of almost four. Tightening the diagnostic criteria to account for one more nonspecific autonomic symptom decreased the number of patients with major depression by only three; adding two more criteria decreased the number by only five. Thus, the rate of DSM-III major depression was 1% higher than the rate with one extra nonspecific autonomic symptom and 2% higher than the rate with two extra criteria. Conversely, loosening diagnostic criteria to account for denial of depressive illness increased the rate of major depression by only 5%. **Conclusions:** Both autonomic and psychological depressive symptoms are strongly associated with depressed mood in acute stroke patients.

(Am J Psychiatry 1991; 148:1172-1176)

In previous publications (1, 2), we have reported that the syndrome of major depression is common among patients with stroke and that lesions in the left frontal cortex or left basal ganglia are more likely to be associated with major depression than lesions in any other brain areas. In addition, previous studies have found that patients with major depression following stroke

are similar to patients with functional depression (i.e., major depression with no known organic etiology) in phenomenology (3), response to dexamethasone (4, 5), cognitive impairment related to depression (6), natural course of untreated depressive disorder (7), and response to antidepressant medications (8-10).

Questions remain, however, about whether the same diagnostic criteria that are used in patients with functional major depression should be used in stroke patients because symptoms used for the diagnosis of depression may occur in medically ill patients independent of depression. For this reason, some investigators have suggested that stroke patients with changes in appetite, sleep, or sexual interest as a result of their medical illness may be "overdiagnosed" as having major depression (11). Conversely, some investigators have suggested that depression may be underdiagnosed in stroke patients who deny symptoms of depression because of anosognosia, neglect, or aprosody (12).

Since, to our knowledge, no previous investigators have systematically examined this issue, this study was

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Supported in part by Research Scientist Award MH-00163 to Dr. Robinson and grant MH-40355 from NIMH, grants NS-15080, NS-92302, and NS-16332 from the National Institute of Neurological and Communicative Disorders and Stroke, and a Young Investigator Award to Dr. Starkstein from the National Association for Research in Schizophrenia and Affective Disorders.

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designed to determine how frequently depressive symptoms occur in acute stroke patients with depressed mood compared with acute stroke patients without mood disturbance to estimate how often diagnostic errors of inclusion or exclusion may be made.

METHOD

The subjects of this study were 205 patients consecutively hospitalized at the University of Maryland Hospital with thromboembolic or hemorrhagic lesions. Patients were excluded if they had a low level of consciousness, moderate to severe comprehension deficit, or did not give informed consent.

Interviews were conducted within the first 2 weeks of admission. Neurological evaluations were done by one of us (T.R.P.), who was blind to the psychiatric findings, using the standardized Stroke Data Bank Examination of the National Institute of Neurological and Communicative Disorders and Stroke (13). The psychiatric examination included the Hamilton Rating Scale for Depression (14) and a structured interview using the Present State Examination (PSE) (15). The PSE was modified to include primarily items related to depression or anxiety and was used to make DSM-III-based diagnoses described in a previous publication (16). Cognitive impairment and activities of daily living were assessed by using the Mini-Mental State Examination (17) and the Johns Hopkins Functioning Inventory (18).

Symptoms of depression were divided into autonomic and psychological as described by Davidson and Turnbull (19). No attempt was made to determine whether the symptoms resulted from the patient's medical illness, medications, hospital environment, depression, or other possible causes. CT scans were evaluated by one of us (S.E.S.), as described in a previous publication (2). Intergroup comparisons of parametric data were done with two-tailed *t* tests and appropriate analyses of variance (ANOVAs). Nonparametric data were compared by using chi-square tests.

RESULTS

Background Characteristics

The study group consisted of 205 patients with a mean±SD age of 58.7±13 years; 131 (64%) were black, 107 (52%) were men, 96 (47%) were married, and 135 (66%) were from Hollingshead class IV and V. Eighty-five (41%) of the patients reported having depressed mood, and 120 (59%) reported no mood disturbance. There were no statistically significant differences between the patients with and without depressed mood in terms of sex, race, socioeconomic status, marital status, personal or family history of psychiatric disorder, previous medical history, or medications taken at the time of the interview. However, the group with depressed

mood was younger than the group without mood disturbance (56.5±12 years compared with 60.4±14 years, respectively) ($t=-2.08$, $df=203$, $p=0.04$) and had lower scores on the Mini Mental State (22±5.6 versus 24±4.8) ($t=-1.96$, $df=203$, $p=0.05$). The group with depressed mood also had higher Hamilton depression scores (13±6.5 versus 5.0±5.6) ($t=9.37$, $df=203$, $p<0.001$) and higher Johns Hopkins Functioning Inventory scores (7.3±5.7 versus 5.3±5.8) ($t=2.53$, $df=203$, $p=0.012$).

Neurological and Neuroradiological Findings

The site of the brain lesion was based on CT for 125 of the patients and on clinical findings for 80 (both findings were available for some of the patients). Among the 85 patients with depressed mood, 30 (35%) had right and 46 (54%) had left hemisphere stroke and nine (11%) had other lesion locations (e.g., posterior circulation territory or bilateral). In the group without mood disturbance, 70 (58%) had right, 36 (30%) had left, and 14 (12%) had other lesion locations. The difference between groups in lesion location was significant: $\chi^2=12.47$, $df=2$, $p<0.01$. On individual comparisons, significantly more of the group with depressed mood than the group without mood disturbance had left hemisphere lesions ($\chi^2=9.83$, $df=1$, $p<0.01$). There were no statistically significant intergroup differences in the rate of thromboembolic or hemorrhagic strokes, involvement of any particular brain structures, or severity of motor, sensory, visual, or language deficits.

Autonomic and Psychological Symptoms

The psychological and autonomic symptoms of patients in the two groups are shown in table 1. For further analysis, the number of psychological and autonomic symptoms for each patient was converted to a Z score to control for the difference in number of symptoms in each category. The groups were then compared by using a two-way ANOVA with the factors of the presence or absence of depressed mood and autonomic or psychological symptom Z scores. The only significant factor was presence or absence of depressed mood ($F=7.981$, $df=1$, 203 , $p=0.005$) (i.e., the autonomic and psychological symptom scores were significantly higher in the group with depressed mood than in the group without mood disturbance). There was no effect for type of symptom (i.e., autonomic symptom scores were not significantly different from psychological symptom scores), and there was no interaction between factors (e.g., the group without mood disturbance did not have higher autonomic than psychological symptom scores). When we controlled for age, Mini Mental State score, and Johns Hopkins Functioning Inventory scores by matching for these variables, a significant effect was found only for depressed versus nondepressed status. We also compared 12 patients with depressed mood and five patients without mood disturbance who had left anterior lesions (i.e., locations previously associated with major depression). We again found a sig-

TABLE 1. Autonomic and Psychological Symptoms in Acute Stroke Patients With and Without Depressed Mood

Symptom	With Depressed Mood (N=85)		Without Depressed Mood (N=120)		p ^a
	N	%	N	%	
Autonomic					
Anxiety	42	49	12	10	<0.001
Anxious foreboding	34	40	11	9	<0.001
Morning depression	48	56	9	8	<0.001
Weight loss	33	39	19	22	<0.01
Delayed sleep	37	44	25	21	<0.01
Subjective anergia	48	56	29	24	<0.001
Early awakening	28	33	22	18	n.s.
Loss of libido	35	41	12	10	<0.001
Psychological					
Worrying	59	69	83	23	<0.001
Brooding	36	42	8	7	<0.001
Loss of interest	22	26	5	4	<0.001
Hopelessness	41	48	16	13	<0.001
Suicidal plans	15	18	1	1	<0.001
Social withdrawal	31	36	10	8	<0.001
Self-depreciation	23	27	7	6	<0.001
Lack of self-confidence	19	22	7	6	<0.01
Simple ideas of reference	32	38	10	8	<0.001
Guilty ideas of reference	23	27	8	7	<0.01
Pathological guilt	20	24	10	8	<0.05
Irritability	34	40	13	11	<0.001

^aBonferroni corrected.

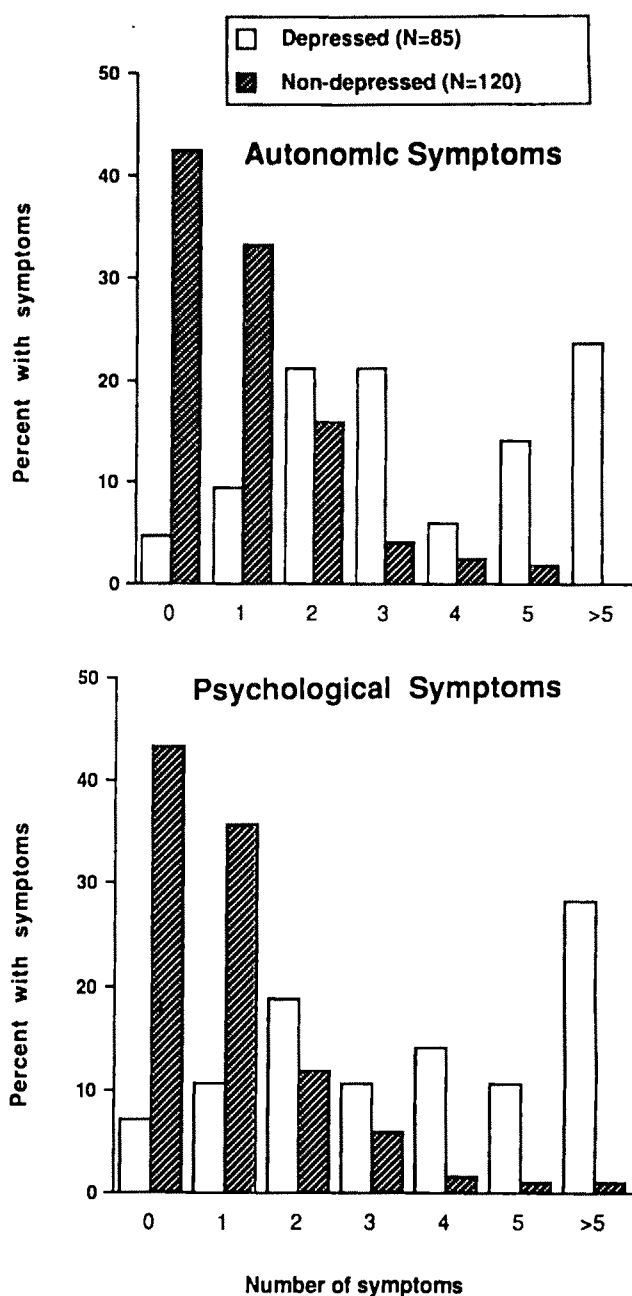
nificant effect only for depressed mood ($F=15.67$, $df=1$, 15 , $p<0.001$).

Specificity of Diagnostic Criteria

The 85 patients with depressed mood had significantly more autonomic symptoms than the 120 patients without mood disturbance (3.63 ± 2.14 versus 0.96 ± 1.12) ($t=11.66$, $df=203$, $p<0.001$); they also had more psychological symptoms (4.12 ± 2.82 versus 0.94 ± 1.2) ($t=11.05$, $df=203$, $p<0.001$). The frequency distributions are shown in figure 1. The only symptom that was not significantly more frequent in the group with depressed mood than in the group without mood disturbance was early morning awakening (table 1).

The adequacy of *DSM-III* criteria in this group of medically ill patients was assessed first by determining whether major depression was overdiagnosed. Forty-six of the 205 patients were assigned a *DSM-III* diagnosis of major depression. Adding one extra autonomic symptom to the minimum required by *DSM-III* changed the diagnosis from major depression to no major depression in only three of these patients; adding two extra criteria changed the diagnosis in five. Thus, the rate of major depression according to *DSM-III* criteria—22%—was 1% higher than the rate with one extra non-specific autonomic symptom—21%—and 2% higher than the rate with two symptoms—20%.

A second question is whether major depression was underdiagnosed because some patients were unable or unwilling to acknowledge their depressed mood. To an-

FIGURE 1. Prevalence of Autonomic and Psychological Symptoms in Acute Stroke Patients With and Without Depressed Mood^a

^aThe frequency of symptoms among the patients without mood disturbance appears to be a smooth unimodal distribution, but the distribution among depressed patients may be bimodal. Most of the depressed patients with five or more autonomic symptoms had major depression ($N=27$) rather than minor depression ($N=2$). Significantly more of the patients with major depression than those with minor depression had more than four symptoms ($\chi^2=13.4$, $df=1$, $p<0.001$).

swer this question, we determined how many patients failed to meet diagnostic criteria for major depression only because they denied having a depressed mood. There were 10 such patients. The mean scores of these patients on the Mini-Mental State (22 ± 7) and the Johns

TABLE 2. Characteristics of Acute Stroke Patients Who Met All DSM-III Criteria for Major Depression or All DSM-III Criteria Except Depressed Mood

Characteristic	Met All Criteria (N=46)		Met All Criteria Except Depressed Mood (N=10)	
	N	%	N	%
Male	18	39	3	30
Black	27	59	7	70
Married	18	39	5	50
Hollingshead social class I-III	11	24	5	50
Lesion location				
Left hemisphere ^a	25	54	1	10
Right hemisphere ^b	15	33	6	60
Other (multiple, brainstem, or cerebellar)	6	13	3	30

^aSignificantly more patients with major depression with depressed mood had left hemisphere lesions ($\chi^2=6.49$, $df=1$, $p<0.01$).

^bThe difference between groups was not significant ($\chi^2=2.63$, $df=1$, $p=0.10$).

Hopkins Functioning Inventory (6 ± 7) did not differ significantly from those of the patients with major depression with depressed mood (22 ± 6 and 8 ± 6 , respectively). However, the 10 patients who met all of the criteria for major depression except depressed mood had a significantly lower mean Hamilton depression score (11 ± 5 versus 17 ± 5) ($t=3.16$, $df=54$, $p<0.003$). In addition, significantly fewer of these 10 patients had left hemisphere lesions (table 2). However, the hypothesis that more patients with major depression without mood disturbance than those with depressed mood would have right hemisphere lesions was not supported (table 2). In addition, when the 10 patients with "masked" depression were added to the group of patients with "acknowledged" depression, our previous finding that more patients with depression had left hemisphere lesions than right hemisphere lesions remained statistically significant ($\chi^2=7.93$, $df=1$, $p<0.01$).

DISCUSSION

The major finding of this study is that both autonomic and psychological depressive symptoms are strongly associated with depressed mood in patients with acute stroke. Patients without mood disturbance had a mean of one autonomic symptom, compared with a mean of almost four symptoms in the depressed group. However, altering the diagnostic criteria to account for the baseline rate of one autonomic symptom resulted in less than a 2% decrease in the frequency of major depression. Finally, only 5% of the patients with acute stroke had all the necessary symptoms for major depression except depressed mood.

Before discussing the implications of this study, it is important to note its limitations. This study was conducted in a predominantly black population from middle

and lower socioeconomic classes, and patients with severe comprehension deficits were not evaluated. In addition, small or developing lesions may have been missed because not all patients had positive CT scans at the time of the study. Although it is not obvious how any of these factors would influence our findings, the generalizability of these results to other groups of stroke patients or to other medically ill patients remains to be determined.

Given these limitations, this study has shown that autonomic symptoms of depression are not common among acutely ill stroke patients unless they also have depressed mood. Although clinical psychiatrists are often faced with the task of differentiating physical from mental symptoms, to our knowledge this is the first study to systematically investigate the frequency of depression in a medical illness (stroke) and determine the influence of symptoms associated with acute medical illness on DSM-III criteria for depression. In fact, although it may be possible in some cases to differentiate between symptoms due to depression and those due to medical illness, this study suggests that this distinction is usually not necessary. The low rate of autonomic symptoms of depression in nondepressed acute stroke patients should rarely "create" an otherwise undiagnosed case of major depression.

Of 205 patients, we found only 10 who would meet criteria for major depression if depressed mood were not a required symptom. Although these findings do not refute the interesting hypothesis that some patients who do not acknowledge feelings of sadness following a stroke may be depressed (if worthlessness and guilt were regarded as evidence of depression, only one patient would have remained in this group), they do suggest that, if there are "masked" depressions, they occur in a minority of patients (i.e., less than 5%) and that they are not completely masked (i.e., patients do not deny all psychological symptoms of depression).

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Hypersomnia in Bipolar Depression: A Comparison With Narcolepsy Using the Multiple Sleep Latency Test

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Objective: This study characterized objectively the hypersomnia frequently seen in the depressed phase of bipolar affective disorder. On the basis of previous work in sleep and affective disorders, it has been hypothesized that the hypersomnia is related to greater REM sleep. This hypothesis was tested by using a multiple sleep latency test to compare bipolar affective disorder with narcolepsy, a well-defined primary sleep disorder associated with known REM sleep dysfunction. **Method:** Twenty-five bipolar depressed patients were selected on the basis of complaints of hypersomnia. They underwent 2 nights of polysomnography followed by a multiple sleep latency test. Data on their nocturnal sleep and daytime naps were compared with similar data on 23 nondepressed narcoleptic patients referred for sleep evaluation. **Results:** Despite their complaints of hypersomnia, no abnormalities were noted for the bipolar group in the results from the multiple sleep latency test. Contrary to the working hypothesis, REM sleep was notably absent during daytime naps in the depressed patients, in marked contrast to the findings for the narcoleptic group. **Conclusions:** The complaint of sleepiness in the hypersomnic bipolar depressed patient appears to be related to the lack of interest, withdrawal, decreased energy, or psychomotor retardation inherent in the anergic depressed condition, rather than an increase in true sleep propensity or REM sleep propensity. (Am J Psychiatry 1991; 148:1177-1181)

Although hypersomnia is considered an atypical symptom of affective disorders, it is relatively common in younger depressed patients, particularly those with bipolar affective disorder (1-3). Little information is available to assist the clinician in evaluating this complaint. Can measurable correlates of a complaint of hypersomnia be determined with traditional methods of assessing sleepiness? What is the biological nature of the complaint? Is it similar to any other well-documented disorders involving sleepiness? The answers to these questions may provide a window on the pathophysiology of the anergia that can characterize the depressed phase of bipolar affective disorder and, eventually, may aid in developing specific treatment approaches.

In a previous report (4), we noted an unusually high

percentage of REM sleep in patients with anergic bipolar depression. Some evidence (5, 6) also suggests that the anergic phase of bipolar depression may respond preferentially to treatment with more alerting REM-suppressing antidepressants, such as the monoamine oxidase inhibitor (MAOI) tranylcypromine. The constellation of hypersomnia, high REM sleep indices, and responsiveness to alerting REM-suppressing antidepressants led us to hypothesize that objective measures of hypersomnia in depressed bipolar patients are similar to those in patients with narcolepsy, a clinical sleep disorder characterized by hypersomnia and pathological manifestations of REM sleep (7). Although psychostimulants are the mainstay of narcolepsy treatment, some patients also benefit from MAOIs (8).

We therefore prospectively used the multiple sleep latency test to evaluate a group of bipolar outpatients who were experiencing a current episode of hypersomnic depression. The usefulness of this instrument in assessing states of pathological sleepiness is well established (9). On the basis of our hypothesis that the hypersomnia in bipolar depressed patients has biological similarities to narcolepsy, we compared the profile of the bipolar depressed group with that of a group of

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Supported in part by NIMH grants MH-37266, MH-37869, MH-00295, and MH-30915 and by a grant from the John D. and Catherine T. MacArthur Foundation.

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nondepressed narcoleptic patients concurrently studied in our sleep evaluation center.

METHOD

Our selection of patients with bipolar disorder has been described in a previous report (4). The diagnosis of primary bipolar depression was confirmed with the Research Diagnostic Criteria (RDC) (10) and was based on a semistructured interview conducted by an experienced clinical psychologist and supervised by one of us (M.E.T., J.M.H.). Of the more than 70 eligible bipolar patients who were screened, 56 met the following operational definition of anergic depression: 1) definite anergia (score of 2 on item 13 of the Hamilton Rating Scale for Depression [11]), 2) psychomotor retardation (score of 2 or more on Hamilton item 8), and 3) at least one of two associated reversed neurovegetative features: a) weight gain of 2.2 kg or more or b) hypersomnia, i.e., 1 or more hours of sleep per day more than usual. Among the 56 anergic bipolar depressed patients accepted for treatment in our research clinic, we identified 25 patients with definite hypersomnia, as defined as spending 1 or more hours more in bed each day than usual and napping more than 30 minutes most days. Their mean \pm SD level of severity on the first 17 items of the Hamilton scale after a 14-day evaluation period was 19.7 \pm 5.7.

The mean \pm SD age of these 25 hypersomnic bipolar patients (10 men and 15 women) was 36.6 \pm 11.9 years, and the mean \pm SD length of their current episodes of depression was 14.8 \pm 9.2 weeks. The mean \pm SD number of prior depressive episodes was 7.7 \pm 6.7, and the mean \pm SD number of prior hypomanic/manic episodes was 5.4 \pm 5.8. According to the RDC, 13 patients met the criteria for bipolar I disorder and 12 were classified as having bipolar II disorder; no patient was experiencing four or more episodes per year at the time of intake into the trial.

The comparison group consisted of 23 narcoleptic patients (nine men and 14 women). The narcoleptic patients had been referred to our sleep evaluation center over 2 years for evaluation of excessive daytime somnolence. The referred patients were screened to exclude patients with concurrent RDC diagnoses of alcoholism or drug abuse, borderline or antisocial personality disorder, mental retardation, schizophrenia, schizoaffective disorder, seizure disorder, episode of psychotic major depression, or unipolar or bipolar affective disorder; the final diagnoses were made by one of us (C.F.R.) in accordance with the Association of Sleep Disorders Centers' classification of sleep and arousal disorders (12). The mean \pm SD age of the 23 narcoleptic patients was 42.2 \pm 11.4 years. The age difference between our narcoleptic and bipolar groups did not reach statistical significance ($t=-1.66$, $df=46$, $p=0.10$). Cataplexy, sleep paralysis, and hypnagogic hallucinations were reported in 14, 12, and 14 narcoleptic patients, respectively.

The bipolar patients and narcoleptic patients received similar evaluations with all-night EEG and the multiple sleep latency test. A 2-week drug- and alcohol-free washout period was observed. The EEG sleep studies were completed over 2 consecutive nights in our outpatient sleep evaluation center. Our methods for conducting and scoring EEG sleep studies have been published elsewhere (13). Since our primary interest in this study was characterizing the daytime hypersomnia of our bipolar group, sleep variables were selected with the intent of documenting an adequate duration and quality of nocturnal sleep and of identifying any higher REM sleep indices in the depressed group. These variables included mean \pm SD sleep latency, time spent asleep, sleep efficiency, REM latency, REM percent, and REM density (13). All subjects normally retired to their rooms and the lights were turned off by 11:30 p.m. They were allowed to sleep until 7:00 a.m. the next morning.

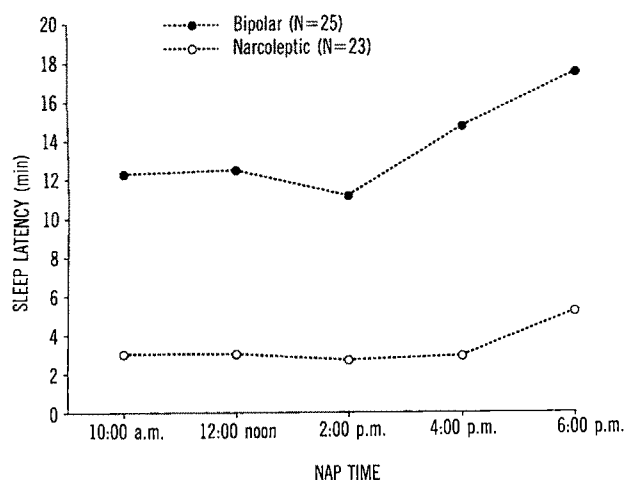
Naps were recorded at 10:00 a.m., 12:00 noon, 2:00 p.m., 4:00 p.m., and 6:00 p.m. on the day after the second night of polysomnography. The daytime nap studies consisted of EEG (C3/A2), referential electro-oculogram, and submental bipolar electromyogram. Our procedures for conducting multiple sleep latency test studies have been reported elsewhere (14). The sleepiness index was defined as 100 - (sum of sleep latencies for five naps). Sleep-onset REM periods were defined as REM periods within 10 minutes of sleep onset. Nap studies for patients who fell asleep during the nap period were scored in accordance with standard criteria (15). When a subject did not fall asleep during the daytime nap, the sleep latency was recorded as 20 minutes.

EEG sleep variables were analyzed by a series of two-tailed t tests to assess differences between the bipolar and narcoleptic groups in 2-night averaged data. A Fisher's exact probability was calculated to compare the prevalences of sleep-onset REM periods in the two groups. Nap data were analyzed by repeated measures analyses of variance (ANOVAs), with diagnosis as the group effect and nap period as the repeated measure. On variables showing significant Group by Nap interactions, a profile contrast within each group was performed on the nap data to identify the nap period in which the change occurred.

RESULTS

All-Night Sleep Studies

The bipolar patients appeared to have an adequate duration (385.5 \pm 66.7 minutes) and quality (sleep efficiency=86.1 \pm 8.6%) of nocturnal sleep. They did not fall asleep as quickly as the narcoleptic patients (sleep latency=26.0 \pm 21.3 minutes and 10.5 \pm 15.0 minutes, respectively; $t=2.87$, $df=46$, $p<0.01$). The bipolar patients had a significantly longer nocturnal REM latency than the narcoleptic group (82.4 \pm 33.4 versus 46.5 \pm 40.8 minutes; $t=3.34$, $df=46$, $p<0.002$), a comparable REM

FIGURE 1. Mean Sleep Latency During Naps of Bipolar Depressed Patients With Hypersomnia and Narcoleptic Patients^a

^aSignificant group effect ($F=138.10$, $df=1, 46$, $p<0.0001$), nap effect ($F=10.66$, $df=4, 184$, $p<0.0001$), and Group by Nap interaction ($F=2.49$, $df=4, 184$, $p<0.05$) according to repeated measures ANOVA.

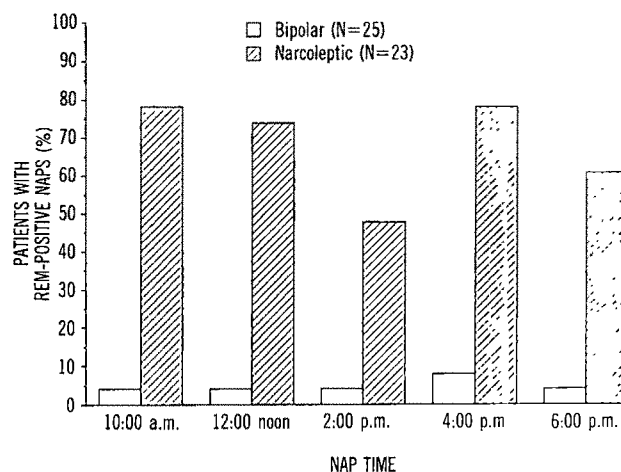
percent ($20.9\pm5.0\%$ versus $22.9\pm5.3\%$, n.s.), and a significantly lower REM density (1.3 ± 0.5 versus 1.7 ± 0.3 ; $t=-2.98$, $df=46$, $p<0.01$).

Nocturnal sleep-onset REM periods were noted in none of the 25 bipolar patients and in eight of the 23 narcoleptic patients (Fisher's exact probability test, $p=0.001$).

Multiple Sleep Latency Test

The bipolar group exhibited relatively normal results on the multiple sleep latency test; there was little evidence of pathological sleepiness (figure 1). No bipolar patient exhibited a sleepiness index of more than 75, i.e., a score indicative of pathological sleepiness, and the mean sleepiness index for the total group of patients was within normal limits (31.5 ± 19.1). Only 20% of the hypersomnic bipolar depressed group fell asleep during all five naps; 24%, 28%, 20%, and 8% fell asleep during four, three, two, and one naps, respectively. Objective sleepiness tended to decrease as the day progressed. By contrast, the nap study profile of the narcoleptic group showed a higher sleepiness index in this group (83.1 ± 9.2 ; $t=12.07$, $df=35$, $p<0.0001$) and a significantly lower sleep latency (figure 1). Twenty-two of the 23 narcoleptic patients fell asleep during all five naps, and the other subject fell asleep during four of the five naps.

The bipolar patients exhibited little REM sleep during the daytime naps (figure 2). Of the 25 hypersomnic bipolar depressed patients, 21 (84%) did not show REM sleep in any of the five naps. Two patients had REM sleep in one nap and two other patients had REM sleep during two naps. In contrast, all of the narcoleptic patients exhibited REM sleep in at least one daytime nap. Of the 23 narcoleptic patients, 21 (91%) exhibited REM sleep in at least two naps.

FIGURE 2. Prevalence of REM-Positive Naps Among Bipolar Depressed Patients With Hypersomnia and Narcoleptic Patients^a

^aOf the 125 naps taken by the bipolar hypersomnic patients, six (5%) were REM positive; the narcoleptic patients took 115 naps, and 78 (68%) were REM positive.

DISCUSSION

The impetus of this comparison of objective measures of sleepiness in hypersomnic depressed bipolar patients and narcoleptic patients was the hypothesis that these groups would have similar objective nap findings regarding sleepiness, attributable in both cases to some REM sleep dysfunction. In fact, we found just the opposite, and this hypothesis must be rejected. The hypersomnia reported in the bipolar depressed state and the hypersomnia of narcolepsy appear to be distinct sleep/wake disorders, as reflected in our comparisons of sleep EEG and multiple sleep latency tests. According to theories distinguishing "REM sleepiness" from "non-REM sleepiness," REM-related naps are associated with a greater propensity for sleep (both objectively and subjectively) and are associated with more restorative sleep (16, 17). Hypersomnia in bipolar depression might represent non-REM sleepiness, in contrast to the REM sleepiness manifested by our narcoleptic group. However, our data did not confirm objective sleepiness in the bipolar depressed group.

The multiple sleep latency test is felt to measure physiological sleep tendency in the absence of alerting factors (18). In normal subjects sleep latency tends to decrease throughout the morning, reaching a minimum at midday and rising to a late afternoon maximum (19). Daytime sleepiness is felt to be affected by five different variables: sleep loss, sleep fragmentation, circadian rhythms, CNS pathology, and drugs (20). Narcolepsy is a disorder of excessive daytime somnolence due to presumed CNS pathology (9, 21–23). This is thought to be a REM sleep dysfunction because of the characteristic nature of REM sleep onset, which distinguishes narcolepsy from other disorders of excessive daytime somnolence. REM-containing naps have been

shown to be associated with both objectively and subjectively higher measures of sleepiness than are naps that do not contain REM sleep (16, 17).

The major findings of this study include the absence of indicators of pathological sleepiness in the bipolar group, despite their unequivocal reports of hypersomnia. In addition, contrary to our working hypothesis of a greater propensity for daytime REM sleep in the hypersomnic bipolar patients, there was no evidence of it.

The nocturnal sleep EEG findings for the bipolar patients do not implicate disrupted nocturnal sleep as an etiology of their reported daytime sleepiness. Nor is REM sleep dysregulation or greater REM sleep propensity apparently implicated as a contributing cause of the hypersomnia in this group. In fact, the narcoleptic patients showed more evidence of depression-like REM abnormalities than the bipolar patients (13).

Our bipolar subjects thus can be considered as having a relatively normal multiple sleep latency test profile, including normal sleep latencies (and absence of sleep in the majority of naps), a relative absence of REM sleep during naps, and a normal circadian distribution of sleepiness across the nap periods. In a previous study from our laboratory (24), 14 healthy young comparison subjects (mean age \pm SD = 23.9 \pm 3.1 years) exhibited multiple sleep latency test findings virtually identical to those of our bipolar group. For example, the healthy comparison subjects had a mean \pm SD sleepiness index of 39.1 \pm 28.6, and only 14 of 137 naps contained REM sleep (24). Our narcoleptic group's multiple sleep latency test profile is similar to the profiles of narcoleptic patients reported in the literature (25, 26); the findings included short sleep latency, high REM sleep measures, and a relative stable circadian distribution of objective sleepiness and REM sleep propensity throughout the naps.

Several possibilities may explain the lack of objective evidence of pathological sleepiness in our bipolar subjects. If one assumes that the multiple sleep latency test is a valid test for this population, one could conclude that complaints of hypersomnia in our bipolar depressed group reflect a more subjective state of anergic depression (i.e., lack of interest, fatigue, and/or withdrawal), rather than a truly greater propensity to sleep. However, our clinical experience suggests that hypersomnic bipolar depressed patients do, indeed, sleep more during the daytime than is suggested by these findings from the multiple sleep latency test. The alternative possibility is that the multiple sleep latency test is an invalid measurement of the type of daytime sleepiness experienced in hypersomnic depression. This test is designed primarily as a marker of sleep initiation. It is possible that hypersomnic bipolar patients, like other depressed patients, have difficulty initiating sleep but that, once sleep is initiated, they spend a significantly larger than normal portion of the day asleep. The multiple sleep latency test artificially disrupts prolonged napping during the daytime and may not reflect this additional proportion of the day spent sleeping. The absence of REM sleep during naps in the hypersomnic bipolar depressed group may also be an artifact of the

artificially brief nap period in the multiple sleep latency test condition. In a previous study by our group (14), when depressed patients were allowed to sleep longer during daytime naps, they were found to have abnormally short REM latencies. The underlying pathophysiology of the hypersomnia complaint in bipolar depression thus remains unclear. The notion of chronic sleep loss based on a greater sleep propensity in the face of difficulty initiating sleep may be entertained. However, this view is limited by the observation that the nocturnal sleep of bipolar patients, if anything, seems to be more consolidated than that of unipolar depressed patients and involves maintenance of slow wave sleep, normal REM latency, and, overall, less disturbed nocturnal sleep continuity (4).

The present study may have several implications for the evaluation of the hypersomnic patient and for the development of theories of hypersomnia in affective disorders. First, the complaint of hypersomnia in a psychiatric population in the absence of objective markers of sleepiness should not be minimized. Future studies will need to address the validity of objective measures to document the sleepiness present in this group, which apparently cannot be identified readily with the multiple sleep latency test. Second, theories on the pathophysiology and treatment of hypersomnic depressions must take into consideration the relative absence of REM sleep propensity apparent during the daytime and, perhaps, address the qualitative appearance of the non-REM sleepiness in this population.

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Social Competence and Positive and Negative Symptoms: A Longitudinal Study of Children and Adolescents at Risk for Schizophrenia and Affective Disorder

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Objective: The authors longitudinally examined social competence and positive and negative symptoms in children at risk for schizophrenia, children at risk for affective disorder, and matched normal subjects. **Method:** The subjects were offspring of parents with schizophrenia or affective disorder and normal comparison subjects matched on age, sex, and socioeconomic status. Ratings of social competence (Premorbid Adjustment Scale), affective flattening and poverty of speech (Scale for the Assessment of Negative Symptoms), and positive formal thought disorder (Scale for the Assessment of Positive Symptoms) were based on videotaped psychiatric interviews conducted in childhood (N=144), early adolescence (N=127), and adolescence (N=106). **Results:** In childhood, there were no significant group differences. In early adolescence, the subjects at risk for schizophrenia had poorer social competence than those at risk for affective disorder and the normal subjects. In early adolescence, the subjects at risk for schizophrenia also had greater positive thought disorder than those at risk for affective disorder but did not differ significantly from the normal subjects; there were no differences in negative symptoms. In adolescence, the subjects at risk for schizophrenia had poorer social competence and greater positive and negative symptoms than the adolescents at risk for affective disorder and the normal subjects. **Conclusions:** During early adolescence and adolescence, poor social competence may be more characteristic of children at risk for schizophrenia than those at risk for affective disorder. Higher levels of positive and negative symptoms may also be specific to subjects at risk for schizophrenia, but only during adolescence.

(Am J Psychiatry 1991; 148:1182-1188)

The distinction between positive and negative symptoms has become increasingly prominent in theory and research on schizophrenia (1-7). In this

research, delusions, hallucinations, and certain types of thought disorder (e.g., incoherence, derailment) are considered positive symptoms and affective flattening and other types of thought disorder (e.g., poverty of speech) are typically considered negative symptoms. Strauss et al. (1, 8) identified a third type of symptom—disorders of social relationships—that has not received much attention in these studies, and they suggested that social functioning reflects a semi-independent longitudinal process in the development of schizophrenia. Although the results of research on genetic influences (9), sex differences (10, 11), and social skills (12) suggest that positive and negative symptoms and social functioning reflect separate underlying processes, the extent to which these three groups of symptoms have different longitudinal paths in the developmental course of schizophrenia remains unclear.

Longitudinal studies have provided data consistent with Crow's suggestion (2, 3) that a predominantly

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Supported in part by grants to Dr. Erlenmeyer-Kimling from NIMH (grants MH-19560 and MH-30921), the W.T. Grant Foundation, and the Scottish Rite Committee for Research on Schizophrenia.

The authors thank Ulla Adamo, M.A., Barbara Maminski, B.A., and Simone Roberts, B.S., for their assistance, Sharon Gordon, Ph.D., for her criticism, and Clarice Kestenbaum, M.D., and her colleagues for conducting the interviews.

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positive symptom syndrome develops into a predominantly negative symptom syndrome in many schizophrenic patients (6). However, few studies have investigated the longitudinal development of positive and negative symptoms and social competence before the onset of diagnosed schizophrenia. In an important series of studies, Knight and Roff (13, 14) explored the interrelationships among affective deficit, social competence, and thought disorder in the development of schizophrenia, using clinical ratings and symptom and social history scales to examine child guidance clinic records, military service records, and Veterans Administration files. In their research, social competence and affective deficit appeared to reflect relatively independent, longitudinally stable processes beginning in childhood; these results provide support for the suggestion of Strauss et al. (1, 8) that social functioning and negative symptoms reflect semi-independent processes in the development of schizophrenia.

In their studies, Knight and Roff (13, 14) used a combination of follow-up and follow-back methods. As is now well appreciated, studies of the offspring of schizophrenic parents provide another means of exploring the longitudinal development of schizophrenic symptoms and signs (15–17). Few studies of high-risk subjects, however, have investigated positive and negative symptoms and social competence concurrently; in a previous report (18), we examined the offspring of parents with schizophrenia and affective disorder and found evidence of dissimilar patterns of group differences in these three types of symptoms during adolescence.

In the present report, positive and negative symptoms and social competence were examined longitudinally in a second, independent group of high-risk offspring by conducting assessments during childhood, early adolescence, and adolescence. For adolescence, we hypothesized that the results of the present analysis would be similar to those presented in our previous report (18), that is, that poor social competence would be specific to subjects at risk for schizophrenia, that positive thought disorder would be greater in both high-risk groups than in normal subjects, and that there would be no group differences in negative symptoms. On the basis of previous research on high-risk subjects (19), we hypothesized that social competence would also be poorer in early adolescents at risk for schizophrenia. Inconsistent results in previous studies precluded hypotheses regarding childhood. Our perspective was the investigation of psychological processes that are important in the development of schizophrenia, not the diagnosis of psychiatric disorder. As Matthyse and Holzman have suggested, in family studies of psychiatric disorder, approaches that maximize information about subclinical manifestations and subtle cognitive, affective, and personality variables are “likely to be much more revealing than epidemiologically-based methods which simply assign individuals to pre-existing diagnostic categories” (20, p. 273).

METHOD

The New York High-Risk Project, a longitudinal investigation of the offspring of parents with schizophrenia and affective disorder, was begun in 1971 by Erlenmeyer-Kimling (21, 22). Two independent subject groups are included in the project; the present analysis was based on the second of these, ascertained in 1977–1979. The study is described in detail elsewhere (21, 22).

From patients consecutively admitted to New York State psychiatric facilities in the New York City metropolitan area, adult patients with intact marriages who had 7- to 12-year-old children with no evident psychiatric disorder or mental retardation were diagnosed according to the Research Diagnostic Criteria (RDC) (23) by two senior psychiatrists using information from hospital records. Only patients for whom there was consensus agreement on a diagnosis of schizophrenia or affective disorder were accepted into the study. Subsequently, these patients were administered the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (24) to confirm the diagnoses based on records. On the basis of comparisons of the major variables examined in the study, the offspring of the parents with schizophrenia and the offspring of the parents with schizoaffective, mainly schizophrenic, disorder were combined, as were the offspring of the parents with affective disorder and schizoaffective, mainly affective, disorder.

A population sampling firm identified a large number of families matched in socioeconomic status to the patient families, from which a group of normal comparison children matched to the high-risk children on age and sex was selected. Children in this group were 7–12 years of age, from intact homes, and without histories of psychiatric problems or mental retardation. Families in which either parent had had psychiatric hospitalization or treatment or a history of psychiatric problems were excluded from this normal comparison group.

The three groups of offspring were assessed at 2- to 3-year intervals with a variety of biobehavioral and clinical measures (21, 22). At the first, second, and third testing rounds, 30-minute semistructured videotaped interviews were administered by child psychiatrists blind to the subjects' group membership and were subsequently rated for psychopathology and adaptive traits on the Mental Health Assessment Form (25) by raters who were also blind to group membership. For the present analysis, ratings of positive and negative symptoms and social competence were carried out with the same methods used in the previous analysis of these dimensions (18) in the first of the two New York High-Risk Project subject groups (21, 22). The interviews from the second and third testing rounds were rated independently and in separate random orders of subjects by each of two raters randomly chosen from three advanced graduate students in clinical psychology who were blind to the subjects' group

TABLE 1. Scores of Children (mean age=9.0 years) at Risk for Schizophrenia or Affective Disorder and of Normal Children on Measures of Social Competence and Positive and Negative Symptoms

Measure ^a	R ^b	Offspring of Parents With Schizophrenia (N=44)		Offspring of Parents With Affective Disorder (N=38)		Normal Comparison Children (N=62)		Analysis	
		Mean	SD	Mean	SD	Mean	SD	F	p ^c
Social competence	0.78	1.55	0.74	1.32	0.69	1.38	0.75	1.14	0.32
Global positive formal thought disorder	0.68	0.23	0.63	0.11	0.29	0.06	0.29	1.94	0.15
Affective flattening	0.71	0.42	0.48	0.38	0.45	0.46	0.59	0.24	0.79
Poverty of speech	0.82	0.90	1.15	0.43	0.85	0.77	1.20	1.91	0.15

^aFor all measures, a higher score reflects greater pathology. The instruments used were as follows: social competence—mean of scores on the items in the Premorbid Adjustment Scale (26); global positive formal thought disorder—Scale for the Assessment of Positive Symptoms (28); affective flattening—mean of scores on four items from the affective flattening subscale of the Scale for the Assessment of Negative Symptoms (SANS) (4); poverty of speech—SANS.

^bIntraclass correlation coefficient for interrater reliability on the mean ratings.

^cConventional significance level based on one-way ANOVA.

membership. The third round interviews, at which the mean age of the subjects was 15.4 years, were rated first. The second round interviews, at which the mean age of the subjects was 12.3 years, were rated 3 months after the third round ratings were completed. The first round interviews, at which the mean age of the subjects was 9.0 years, were rated independently and in separate random orders by two different advanced graduate students in clinical psychology who both had appreciable experience in childhood psychopathology and were also blind to the subjects' group membership.

Social competence was assessed by using the mean of the scores on items of the Premorbid Adjustment Scale (26). We modified the first item of the scale—"sociability and withdrawal"—to reflect sociability and withdrawal observed in the interview, thereby more clearly distinguishing this rating from the second item of the scale, "peer relationships." Affective flattening and poverty of speech have been considered the core of the negative symptom syndrome (3, 6). On the basis of research on affective deficits in schizophrenia (14), affective flattening was assessed by using the mean of the scores on four items (unchanging facial expression, poor eye contact, affective nonresponsivity, and lack of vocal inflection) selected from the affective flattening subscale of the Scale for the Assessment of Negative Symptoms (SANS) (4). Although it could be argued that the SANS anhedonia-asociality subscale is also a measure of affective flattening, ratings on this subscale may reflect a combination of affective flattening and social competence (27); therefore, to keep our ratings of social competence and affective flattening as distinct as possible, items from this subscale were not examined. The poverty of speech rating from the SANS was used to assess this second negative symptom. The positive formal thought disorder global rating from the Scale for the Assessment of Positive Symptoms (SAPS) (28) was used to assess this positive symptom because it was not possi-

ble for us to rate reliably the individual positive thought disorder items from this subscale in children. The remaining positive symptoms from the SAPS—hallucinations, delusions, and bizarre behavior—were not rated because very few of the offspring exhibited them in childhood and adolescence.

RESULTS

The intraclass correlation interrater reliabilities (29) of the means for the two raters who rated each of the measures are presented in tables 1–3 and were generally satisfactory. The tables present the results of one-way analyses of variance (ANOVAs) (including correction for multiple tests of significance with the family-wise multistage Bonferroni procedure [30]) and Tukey-Kramer tests (31) comparing the offspring of parents with schizophrenia and affective disorder and the normal children and adolescents at each of the three ages at which the offspring were interviewed. As can be seen from table 1, during childhood there were no significant differences among the three groups in social competence, positive formal thought disorder, and negative symptoms. Table 2 presents the results for early adolescence. At this age, the offspring at risk for schizophrenia had significantly poorer social competence than the offspring at risk for affective disorder and the normal comparison children. Early adolescents at risk for schizophrenia also had more positive thought disorder than those at risk for affective disorder but did not differ significantly from the normal early adolescents; there were no group differences in negative symptoms at this age. As shown in table 3, the adolescents at risk for schizophrenia had significantly poorer social competence and greater positive thought disorder, affective flattening, and poverty of speech than the adolescents at risk for affective disorder and the normal comparison adolescents.

As can be seen by comparing the three tables, the

TABLE 2. Scores of Early Adolescents (mean age=12.3 years) at Risk for Schizophrenia or Affective Disorder and of Normal Early Adolescents on Measures of Social Competence and Positive and Negative Symptoms

Measure ^a	R ^b	Offspring of Parents With Schizophrenia (N=34)		Offspring of Parents With Affective Disorder (N=38)		Normal Comparison Early Adolescents (N=55)		Analysis	
		Mean ^c	SD	Mean ^c	SD	Mean ^c	SD	F	p ^d
Social competence	0.76	1.81 _{x,y}	0.89	1.25 _x	0.66	1.41 _y	0.67	5.47	0.005
Global positive formal thought disorder	0.61	0.88 _x	1.13	0.26 _x	0.71	0.49	0.74	4.82	0.01
Affective flattening	0.61	1.01	0.76	0.88	0.61	0.98	0.75	0.36	0.70
Poverty of speech	0.56	1.12	1.22	0.67	0.87	0.80	0.93	1.90	0.15

^aFor all measures, a higher score reflects greater pathology. The instruments used were as follows: social competence—mean of scores on the items in the Premorbid Adjustment Scale (26); global positive formal thought disorder—Scale for the Assessment of Positive Symptoms (28); affective flattening—mean of scores on four items from the affective flattening subscale of the Scale for the Assessment of Negative Symptoms (SANS) (4); poverty of speech—SANS.

^bIntraclass correlation coefficient for interrater reliability on the mean ratings.

^cMeans in the same row that share the same subscript differed significantly at $p < 0.05$ in Tukey-Kramer tests.

^dConventional significance level based on one-way ANOVA. The significance levels based on the multistage Bonferroni procedure were $p < 0.05$ for social competence and positive formal thought disorder; differences on the remaining measures were not significant.

TABLE 3. Scores of Adolescents (mean age=15.4 years) at Risk for Schizophrenia or Affective Disorder and of Normal Adolescents on Measures of Social Competence and Positive and Negative Symptoms

Measure ^a	R ^b	Offspring of Parents With Schizophrenia (N=28)		Offspring of Parents With Affective Disorder (N=33)		Normal Comparison Adolescents (N=45)		Analysis	
		Mean ^c	SD	Mean ^c	SD	Mean ^c	SD	F	p ^d
Social competence	0.81	1.95 _{x,y}	0.98	1.36 _x	0.77	1.36 _y	0.77	5.14	0.007
Global positive formal thought disorder	0.43	0.48 _{x,y}	0.70	0.18 _x	0.53	0.10 _y	0.33	5.00	0.009
Affective flattening	0.73	1.10 _{x,y}	0.88	0.62 _x	0.65	0.68 _y	0.59	4.22	0.02
Poverty of speech	0.75	1.43 _{x,y}	1.32	0.52 _x	0.69	0.46 _y	0.66	11.74	0.0001

^aFor all measures, a higher score reflects greater pathology. The instruments used were as follows: social competence—mean of scores on the items in the Premorbid Adjustment Scale (26); global positive formal thought disorder—Scale for the Assessment of Positive Symptoms (28); affective flattening—mean of scores on four items from the affective flattening subscale of the Scale for the Assessment of Negative Symptoms (SANS) (4); poverty of speech—SANS.

^bIntraclass correlation coefficient for interrater reliability on the mean ratings.

^cMeans in the same row that share the same subscript differed significantly at $p < 0.05$ in Tukey-Kramer tests.

^dConventional significance level based on one-way ANOVA. The significance levels based on the multistage Bonferroni procedure were $p < 0.001$ for poverty of speech and $p < 0.05$ for social competence, positive formal thought disorder, and affective flattening.

numbers of subjects who were rated were somewhat different in childhood, early adolescence, and adolescence. This was a result of videotape deterioration and some subject attrition. When the data were reanalyzed with only the subjects who were rated at all three testing rounds, all statistically significant differences presented in the tables remained significant.

To complement these analyses of group differences in childhood, early adolescence, and adolescence, a set of longitudinal analyses was conducted. For each of the measures of social competence and positive and negative symptoms, the correlation between childhood and adolescence scores was calculated separately for each of the three groups; we examined this time interval to approximate as closely as possible the intervals used in previous longitudinal studies of symptoms and social competence in preschizophrenic and high-risk

groups (13, 14, 32, 33). After Bonferroni correction, only one of the differences in these correlations between the two high-risk groups and between each of the high-risk groups and the normal comparison group was significant. This difference between correlations reflected significantly greater longitudinal stability for positive formal thought disorder from childhood to adolescence in the offspring of parents with affective disorder ($r = 0.78$) than in the normal subjects ($r = 0.32$) ($z = 2.91$, $p < 0.05$, two-tailed). Because this was the only group difference in the longitudinal correlations that was significant, the groups were combined and the correlations for each of the four measures between childhood and adolescence were calculated. After Bonferroni correction, the correlations between childhood and adolescence were significant ($N = 104$, two-tailed test) for social competence ($r = 0.30$, $p < 0.05$), affective

flattening ($r=0.25$, $p<0.05$), and positive formal thought disorder ($r=0.48$, $p<0.01$) but not for poverty of speech ($r=0.15$, $p>0.05$). These correlations reflect significant longitudinal stability from childhood to adolescence for social competence, positive thought disorder, and one of the two measures of negative symptoms.

To examine possible sex differences in the results, we conducted a two-way ANOVA for each of the four measures at each of the three ages. No significant Group by Sex interactions were found, a result that has also been reported in previous analyses of high-risk and preschizophrenic subjects (18, 33–35). There were no significant group differences in age, sex, or family socioeconomic status at any of the three ages. In childhood, mean IQ was significantly lower in both high-risk groups than in the normal comparison group; the children at risk for schizophrenia also had a significantly lower mean IQ than the children at risk for affective disorder ($F=18.21$, $df=2, 140$, $p<0.001$). IQ was also tested during adolescence at the third testing round; at this age, IQ was again significantly lower in both high-risk groups than in the normal comparison group ($F=8.53$, $df=2, 83$, $p<0.001$), but the two high-risk groups did not differ significantly. Although it could be argued that these group differences in IQ may play a role in our results, the existing methods for controlling for differences such as these are problematic (36, 37). It is important to emphasize, however, that there were no group differences in social competence and positive and negative symptoms during childhood, when all three groups differed from each other in IQ, and that during adolescence there were significant differences between the two high-risk groups for all of the measures of social competence and positive and negative symptoms but not for IQ.

DISCUSSION

In the present analysis, social competence, positive formal thought disorder, and two negative symptoms— affective flattening and poverty of speech—were assessed at three different ages in the offspring of parents with schizophrenia and parents with affective disorder. None of these dimensions of psychopathology significantly differentiated the groups during childhood, a finding that might be a result of the fact that at the time of the first testing round children with preexisting psychological disorder were excluded from the study. In both early adolescence and adolescence, not only did the subjects at risk for schizophrenia have significantly poorer social competence than the normal comparison subjects—a result that is consistent with prior research on high-risk subjects (19)—they also had significantly poorer social competence than the subjects at risk for affective disorder, a result we also obtained in our previous analysis of a different group of adolescents (18). Poor premorbid social competence may therefore be more characteristic of individuals

who develop schizophrenia than those who develop affective disorder. This conclusion has received support in some studies of children at high risk for affective disorder but not in others (38, 39). In attempting to account for this inconsistency among studies, it has recently been suggested (39) that studies of high-risk subjects which use *DSM-III* criteria (similar to the RDC, which were used in both of our analyses) may be more likely to show differences between offspring of parents with schizophrenia and those of parents with affective disorder. It is also possible that we found differences in social competence between the subjects at risk for schizophrenia and affective disorder because the measure of social competence used in our analyses (26) was based on research with schizophrenic patients; this measure may therefore have greater validity in assessing schizophrenia-specific deficits in social functioning.

In both early adolescence and adolescence, positive formal thought disorder was greater in the subjects at risk for schizophrenia than in those at risk for affective disorder. However, this result provides only provisional support for the specificity of positive formal thought disorder in subjects at risk for schizophrenia. In our previous analysis of this symptom (18), there was no evidence of specificity—both high-risk groups had greater positive thought disorder than the normal comparison group. In addition, in the present analysis the early adolescents at risk for schizophrenia did not differ significantly in positive thought disorder from the normal subjects. Moreover, the low mean scores for each of the three groups at these times suggest that positive thought disorder in high-risk children and adolescents is a subtle phenomenon, one which should be investigated in future research with more sensitive measures than the clinical ratings used in the present analysis.

It has been suggested (40, 41) that positive symptoms may reflect at least two relatively independent dimensions, a disorganization syndrome that includes positive formal thought disorder and a second syndrome consisting of such florid psychotic symptoms as delusions and hallucinations. However, in a recent study of patients with schizophrenia that specifically addressed this question (42), positive formal thought disorder was significantly correlated with delusions and hallucinations and it was concluded that the positive and negative symptom distinction does encompass formal thought disorder (positive thought disorder was assessed by means of ratings drawn from the SAPS, the same scale used in the present analysis). Nevertheless, until the results of additional research are available, it should be recognized that conclusions based on the single positive symptom we have examined—positive formal thought disorder—may not generalize to a positive symptom syndrome consisting of florid psychotic symptoms.

There were no significant group differences in the two negative symptoms we examined— affective flattening and poverty of speech—in childhood or early

adolescence. However, these symptoms did differentiate the high-risk groups during adolescence, a result we did not obtain in our previous analysis of these symptoms in adolescents (18). Because the methods used in the two analyses were similar, it was not expected that the results would differ. Overall, the results of our previous analysis of social competence, positive thought disorder, and negative symptoms in adolescence (18) were more similar to the results we obtained in the present analysis for early adolescence than for adolescence.

At the time of the videotaped psychiatric interviews, the offspring at risk for schizophrenia and affective disorder had not appreciably entered the age period of risk for these disorders. In part, we examined dimensions of psychopathology, rather than diagnoses, for this reason. In addition, a methodological approach that emphasizes the investigation of such dimensions in the relatives of schizophrenic patients (9, 18, 20, 43–45) has seemed valuable to us. Nevertheless, it will be important, in following these offspring into adulthood, not only to continue examining the longitudinal development of these dimensions, but also to investigate specific psychiatric diagnoses. Structured diagnostic interviews are being conducted in ongoing testing rounds at which these offspring are older (45), and these structured interviews will make it possible to assess the extent to which social competence and positive and negative symptoms—alone and in combination—predict psychiatric diagnosis. Although it is likely that the group differences in the present data reflect vulnerability to the development of schizophrenia, it is possible that they are consequences of rearing by schizophrenic parents. Thus, as these subjects proceed through young adulthood into their 30s, it will also be important to determine whether the longitudinal patterns that characterized the offspring at risk for schizophrenia in the present analysis remain characteristic of those necessarily fewer subjects who develop schizophrenia.

The results of our analysis are consistent with a multidimensional approach to the development of schizophrenia (1–3, 8–10). This approach allows the causes, correlates, and consequences of positive and negative symptoms and social competence to be studied in all patients with schizophrenia, not just in the minority of patients who fulfill criteria for predominantly positive or predominantly negative subtypes (5). But the extent to which these dimensions of psychopathology are relevant to a variety of mental disorders or are individually or configurally specific to schizophrenia remains to be determined. Longitudinal studies, for example, have provided evidence that the relationship between poor premorbid social competence and poor outcome is not unique to schizophrenia (8, 46), and psychopharmacological (47) and family (48, 49) studies have provided evidence consistent with a nonspecific dimension of positive symptoms that plays an important role in both schizophrenia and affective disorder. In the present investigation, however, positive and negative

symptoms and poor social competence were specific to adolescents at risk for schizophrenia. It is therefore possible that these dimensions of psychopathology have greater specificity in individuals vulnerable to schizophrenia than in individuals who have already developed the disorder. To address such developmental changes, a longitudinal perspective on the various configurations in which positive and negative symptoms and social competence occur (50) is needed to complement existing research on these dimensions of psychopathology.

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Lateral Ventricle-Brain Ratio and Balance Between CSF HVA and 5-HIAA in Schizophrenia

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Objective: Lateral ventricle enlargement in schizophrenia has been positively correlated with poor premorbid competence, negative symptoms, and poor treatment response and negatively correlated with concentrations of homovanillic acid (HVA), a dopaminergic metabolite. The authors provide further evidence of a reciprocal relationship between lateral ventricle size and dopaminergic activity in schizophrenia. **Method:** They assessed the relationship between lateral ventricle enlargement (ventricle-brain ratio, VBR) and CSF neurotransmitter metabolite concentrations (HVA and 5-hydroxyindoleacetic acid [5-HIAA]) in 45 patients with schizophrenia, 28 with affective disorders (19 patients with major depression and nine with bipolar disorder), and 91 normal comparison subjects. **Results:** No group mean differences were significant. Although individual correlations of VBR with HVA and 5-HIAA were not statistically significant, the ratio of HVA to 5-HIAA was significantly correlated with VBR in the patients with schizophrenia, a finding consistent with dopaminergic-serotonergic balance hypotheses. **Conclusions:** These data suggest that it is the balance between HVA and 5-HIAA rather than their absolute levels which is associated with brain morphology and that this relationship between brain chemistry and morphology may be characteristic of the normal range of functioning for these systems. In other words, independent of whether brain morphology and chemistry differentiate psychopathological from nonpsychopathological states, there may be an orderly relationship between lateral ventricle size and the balance between HVA and 5-HIAA balance that is especially prominent in schizophrenia.

(Am J Psychiatry 1991; 148:1189-1194)

One of the most consistently reported brain morphological findings in schizophrenia has been enlarged lateral ventricle size (1-5). Generally unrelated to duration and course of illness, medication status, or age of the patient, this putative morphological marker has been reported to be associated with poor premorbid competence, poor response to treatment, and negative symptoms (6). There is, of course, an age effect on ventricle size, which increases with age, especially after age 40. However, the reported differences in ventricle-brain ratio (VBR) between schizophrenic patients and com-

parison subjects have not been attributable to age differences, nor has age been correlated with VBR among schizophrenic patients. Furthermore, lateral ventricle enlargement is not specific to schizophrenia: it has been reported in depression, especially psychotic depression (7), as well as in numerous medical and neurological disorders (8).

The functional significance of lateral ventricle enlargement, although typically assumed to reflect nonspecific and diffuse compromise of the organic integrity of the brain, has not been established. It would be informative if brain morphology were related to the still viable dopamine hypothesis, which has undergone several revisions and interpretations over the last decade. One current version posits that increased subcortical dopaminergic activity may underlie positive symptoms of schizophrenia, while cortical dopaminergic underactivity may be related to the negative symptoms of schizophrenia. A second hypothesis proposes that the balance between dopaminergic and serotonergic activity, not their absolute values, is critical in the expression of positive and negative symptoms in schizophrenia (9).

Presented at the 143rd annual meeting of the American Psychiatric Association, New York, May 12-17, 1990. Received Aug. 6, 1990; revision received March 13, 1991; accepted March 27, 1991. From the Department of Psychiatry, Emory University School of Medicine. Address reprint requests to Dr. Lewine, Emory University School of Medicine, Department of Psychiatry, 1711 Uppergate Drive, N.E., Atlanta, GA 30322.

Supported in part by NIMH grant MH-44151 to Dr. Lewine and a grant from the Georgia Department of Human Resources to the Department of Psychiatry, Emory University School of Medicine.

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Direct examination of the relationship between brain morphology and dopaminergic activity has produced a somewhat mixed picture. Several studies have reported a negative correlation between lateral ventricle size and homovanillic acid (HVA), suggesting that dopaminergic activity decreases as ventricle size increases independent of diagnosis (10–14). Others, such as Houston et al. (15), have failed to find a relationship between lateral ventricle size and HVA but have found a negative relationship between the width of the third ventricle and CSF HVA concentrations. To our knowledge, no study has reported a positive relationship between either lateral or third ventricle size and HVA concentrations. That enlargement of ventricle volume may be associated with diffusely dysfunctional brain chemistry is suggested by the fact that lateral ventricle enlargement has also been negatively correlated with the serotonergic metabolite 5-hydroxyindoleacetic acid (5-HIAA) (12, 14).

We offer in this study further evidence of a reciprocal relationship between lateral ventricle size and dopaminergic activity in schizophrenia. Our data suggest that it is the balance between HVA and 5-HIAA rather than their absolute levels which is associated with brain morphology and that this brain chemistry-morphology relationship may be characteristic of the normal range of functioning for these systems. That is to say, independent of whether or not brain morphology and chemistry differentiate psychopathological from nonpsychopathological states, there may be an orderly relationship between lateral ventricle size and the balance between HVA and 5-HIAA that is especially prominent in schizophrenia.

METHOD

Subjects

The subjects for this study were drawn from an ongoing series of patients and normal comparison subjects admitted to our clinical research program. Patients were recruited from state facilities (hospitals and community mental health centers), private inpatient and outpatient institutions, and private practices through a statewide referral network directed by a full-time doctoral level social worker (R.D.J.). Normal subjects were solicited through newspaper advertisements and word of mouth. An initial screening, either by telephone or in person, reduced to a minimum the number of individuals who were ultimately dropped because of medical complications, positive drug screens, or diagnoses of psychiatric illness.

After appropriate written informed consent was obtained, each individual underwent a thorough physical examination, standard laboratory studies, EEG, EKG, and a drug/medication screen. Extrapyramidal symptoms and tardive dyskinesia were assessed in the patients. All subjects were interviewed with a semistructured psychiatric interview (the Schedule for Affective

Disorders and Schizophrenia—Lifetime Version [16]) to determine current and past psychiatric status and psychosocial history. Further information was obtained from informants and past medical records.

The normal comparison subjects in this analysis had no personal history of major psychiatric illness, nor did any of their first-degree relatives. The final study group for whom we had CSF data comprised 45 patients with schizophrenia, 19 patients with major depression, nine patients with bipolar disorder, and 91 normal comparison subjects. All diagnoses were based on *DSM-III* discharge consensus diagnoses. The depressed and bipolar patients were combined in this analysis because their separation did not change the results. VBR values were available for 23 patients with schizophrenia, 19 patients with affective disorders, and 68 normal comparison subjects.

Measures

VBR. Brain images were made on a Philips GyroScan 1.5-T magnetic resonance imager (the initial series of subjects was run on a 0.5-T scanner; magnet strength had no effect on either tracer reliability or group mean VBRs). Transaxial slices 8-mm thick with an interslice factor of 1.2 were used for the planimetric analyses reported here. They were obtained with spin echo sequences with a short and long echo (repetition time about 2000, echo times about 50 and 100), thereby yielding both T_1 - and T_2 -weighted images. A single T_2 -weighted transaxial slice, the one yielding the largest view of the lateral ventricles, was identified for analysis. We also acquired sagittal and coronal slices but chose to begin our analyses with axial-based data to make our data comparable to most of the CT scan lateral ventricle research from which magnetic resonance imaging studies emerge historically, conceptually, and empirically.

Tracers who were blind to all other information about the subject made three separate tracings of the lateral ventricles; once a tracing was made, all quantitative analyses were conducted automatically by computer. The mean of the three tracings was used as the independent measure. Computer-assisted planimetric procedures automatically yielded a whole brain area for the same slice. By convention, VBR is expressed as ventricle divided by whole brain area multiplied by 100.

Before tracing scans for analysis, the tracers underwent a week-long training program in identifying the appropriate slice and practicing planimetric procedures. Two tracers then jointly traced 10 subjects, the VBRs for which yielded an intraclass correlation (ICC) of 0.94; an additional six jointly traced scans yielded an ICC of 0.82. The drop in ICC was due to a single subject for whom there was considerable disagreement about the location of the lateral ventricle edges; this disagreement was resolved by consensus. The two individuals then traced the remaining scans, submitting their work weekly for review by a senior investigator (R.R.J.L.). Tracers had almost identical means and

TABLE 1. Age, Age at First Admission, Height, and Weight of Subjects With and Without Psychiatric Diagnoses

Diagnostic Group	Age (years) ^a		Age at First Admission (years) ^b		Height (inches) ^c		Weight (lb) ^d	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Patients with schizophrenia (N=45)	34.4	6.8	21.3	5.8	69.1	3.8	176.9	38.3
Patients with affective disorders (N=28) ^e	41.6	10.2	33.3	11.4	68.8	4.1	168.8	35.2
Normal comparison subjects (N=91)	32.8	8.9	—	—	66.8	3.9	152.0	30.3

^aF=11.22, df=2, 164, p<0.001.^bF=35.34, df=1, 71, p<0.001.^cF=5.43, df=2, 154, p=0.005.^dF=8.83, df=2, 155, p=0.002.^ePatients with affective disorders were significantly older than either patients with schizophrenia or normal comparison subjects (Scheffé multiple range test, p<0.05).

standard deviations for the subjects they both traced, indicating absence of tracer bias.

CSF Assays. All subjects were medically healthy, as determined by history and by physical and laboratory examinations, and none was a drug user, as determined by history and urine toxicology screens. Patients had been medication free for a mean of 7 days at the time of testing.

All subjects were hospitalized overnight on our clinical research unit. At 7:30 a.m., research lumbar punctures were done. Twelve cc of CSF was obtained from the L4-L5 interspace with the patient in a lateral decubitus position. CSF 5-HIAA and HVA were determined by high performance liquid chromatography with electrochemical detection.

CSF catechol and indole metabolites of 5-HIAA and HVA were determined by high performance liquid chromatography with electrochemical detection as described by Scheinin (17), with some modifications. The chromatographic apparatus consisted of a BAS 200 (Bioanalytical System) with a glassy carbon working electrode, a Gilson (model 231) autoinjector with a 200- μ l sample loop, a Beckman Ultrasphere ODS-C18 (5- μ particle size) 4.6 mm by 25 cm Chromatographic column, and an Upchurch guard column dry packed with Perisorb RP-18 30-40- μ pellicular packing.

The mobile phase consisted of 0.1 M sodium acetate buffer, 6% methanol, 100 mg/liter EDTA, pH to 5.18 with citric acid. A mixture of 300 μ l of CSF and 30 μ l of internal standard (5-fluoro-homovanillic acid) (2.5 μ m) was passed through the MPS-1 ultrafiltration system of Amicon. A 50- μ l sample was injected onto the column.

The intra- and interassay coefficients of variation for 5-HIAA and HVA of our laboratory were 2.6% and 4.2% and 7.2% and 6.7%, respectively. The limit of detections was below 0.5 pmol/ml.

To assess the effect of washout duration on CSF measures, we examined CSF HVA and 5-HIAA for a subset of 38 patients for whom we had detailed medication histories before admission. The number of days off medication (antipsychotic medication for 33 of the patients) ranged from 4 (N=1) to 4,745 (N=1); 21 (55%) of the patients followed the protocol of 7 days

off medication. The Pearson correlations between number of days off medication and HVA, 5-HIAA, and the ratio of HVA to 5-HIAA were -0.08, -0.06, and -0.11, respectively. The Spearman correlations for these measures were 0.12, 0.11, and -0.11. Neither type of correlation was significant for any measure.

Because the number of days off medication were not normally distributed and to capitalize on extreme groups we divided the patients into four washout duration groups: 1) 24 patients off medication for 7 days or less (mean \pm SD=6.75 \pm 0.74 days), 2) nine patients off medication for more than 7 but less than 30 days (8.67 \pm 16.6), 3) two patients off medication for 30 or 31 days (30.5 \pm 0.71, N=2), and 4) three patients off medication for more than 31 days (2310.75 \pm 2058.78). These four groups did not differ significantly in mean HVA, 5-HIAA, or ratio of HVA to 5-HIAA values. It appears from our results that duration of medication washout and CSF concentrations of HVA and 5-HIAA, and their ratio, were minimally correlated cross-sectionally.

RESULTS

The patients with schizophrenia, the patients with affective disorders, and the normal comparison subjects did not differ significantly by race: 39 (87%) of the patients with schizophrenia, 25 (89%) of the patients with affective disorders, and 65 (71%) of the normal comparison subjects were white. These groups did differ significantly by sex, however: 32 (71%) of the subjects with schizophrenia were men, compared with seven (25%) of the subjects with affective disorders and 40 (44%) of the normal comparison subjects ($\chi^2=15.102$, df=2, p<0.01). Not surprisingly, therefore, the schizophrenic patients were also significantly taller and heavier than the other groups (table 1). Patients with schizophrenia were also significantly younger than patients with affective disorders at first hospital admission (table 1).

The mean HVA, 5-HIAA, ratio of HVA to 5-HIAA, and VBR for the patients with schizophrenia, major depression, or bipolar disorder and the normal compari-

TABLE 2. CSF HVA and 5-HIAA Concentrations, Ratio of HVA to 5-HIAA, and Lateral Ventricle-Brain Ratio (VBR) in Subjects With and Without Psychiatric Diagnoses^a

Diagnostic Group	HVA ^b		5-HIAA ^c		HVA: 5-HIAA ^d		VBR ^e	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Patients with schizophrenia (N=45)	162.8	75.3	97.4	31.2	1.79	0.64	8.9	2.2
Patients with major depression (N=19)	159.3	72.3	97.4	42.2	1.67	0.40	8.9	2.9
Patients with bipolar disorder (N=9)	171.8	83.4	99.5	32.8	1.70	0.57	8.1	1.6
Normal comparison subjects (N=91)	160.6	69.7	90.9	36.0	1.81	0.50	8.8	1.9

^aFor VBR, N=23 for patients with schizophrenia, N=12 for patients with major depression, N=7 for patients with bipolar disorder, and N=68 for normal comparison subjects.

^bF=0.05, df=3, 106, p=0.95.

^cF=0.01, df=2, 159, p=0.99.

^dF=0.15, df=2, 158, p=0.86.

^eF=0.31, df=3, 158, p=0.74.

TABLE 3. Correlations Between Sociodemographic Measures and CSF HVA and 5-HIAA Concentrations, Ratio of HVA to 5-HIAA, and Lateral Ventricle-Brain Ratio (VBR) in 45 Patients With Schizophrenia, 28 Patients With Affective Disorders, and 91 Normal Comparison Subjects^a

Sociodemographic Measure	HVA		5-HIAA		HVA:5-HIAA		VBR	
	r	df	r	df	r	df	r	df
Sex	-0.01	163	0.28 ^b	162	-0.14	162	-0.01	110
Age	0.06	163	0.10	162	-0.09	162	-0.13	110
Age at first admission ^c	-0.03	72	0.13	71	-0.08	71	-0.22	42
Height	-0.05	153	-0.28 ^b	152	0.16	152	-0.05	69
Weight	0.09	154	0.05	153	0.03	153	0.09	70

^aFor VBR, N=23 for patients with schizophrenia, N=19 for patients with affective disorders, and N=68 for normal comparison subjects.

^bp<0.01.

^cPatients with schizophrenia and affective disorders only.

son subjects are given in table 2. No mean group differences were statistically significant.

Table 3 presents the Pearson correlations between sociodemographic variables and the brain measures. The only statistically significant correlations were between 5-HIAA and sex and height, and these were minimally explanatory (they explained less than 10% of the variance). These modest relationships had no effect on the results reported here; the more general issue of gender differences in brain chemistry as it bears on psychopathology will be explored in a separate article.

Correlation matrixes for morphology and chemistry variables for the patients with schizophrenia, the patients with affective disorders, and the normal comparison subjects are presented in table 4. There was a negative correlation between VBR and the ratio of HVA to 5-HIAA in all three groups; the correlation reached statistical significance in the group with schizophrenia (table 4). Visual examination of the scatter plot failed to reveal outliers that might account for the correlation. The independent relationships of HVA and 5-HIAA to VBR were not statistically significant and were of approximately equal magnitudes, suggesting that both measures contributed to the ratio finding.

Finally, we used number of years of education as an index of premorbid social competence (18) and found that the normal comparison subjects had a significantly greater mean number of years of education (15.3 ± 2.5) than either the patients with schizophrenia (13.0 ± 2.3)

or the patients with affective disorders (13.6 ± 2.9) ($F=11.312$, $df=2$, 135 , $p<0.001$). Education did not, however, correlate significantly with HVA ($r=-0.14$, $df=136$), 5-HIAA ($r=-0.07$, $df=136$), or the ratio of HVA to 5-HIAA ($r=-0.13$, $df=136$).

DISCUSSION

Our data are generally consistent with the view that larger ventricles are associated with inferred decreases in dopamine activity; however, rather than an absolute relationship, this may be best described as a relative decrease in comparison with 5-hydroxytryptamine (serotonin) activity (9). Furthermore, since the inverse relationship between lateral ventricle size and HVA and 5-HIAA activity was found within each of the groups (albeit of varying magnitude), it may be a general characteristic not related to specific diagnostic groups or biochemical states. What does appear to be associated with psychopathology (or, more precisely, with possible brain abnormality as reflected in increasing ventricle size) is an exaggeration of this putative dopaminergic-serotonergic relationship.

Four primary methodological factors could contribute to our findings. First, despite the respectable sizes of our study groups, the large number of correlations computed always dictates caution in interpretation, although we note in rejoinder that the relationship of interest (ventricle size and the ratio of HVA to 5-HIAA)

is in the same direction, if not of the same magnitude, for all groups.

Second, lumbar gradient seems unlikely as an interpretation because we would have expected HVA and 5-HIAA to exhibit the same relationship to brain morphology as did their ratio. Furthermore, lumbar gradient would more likely have affected absolute metabolite levels, which did not differ significantly among our groups. Height did not correlate significantly with any of the metabolite measures, providing additional evidence against the gradient explanation.

Third, only large changes in brain metabolite turnover are likely to be detected with CSF assay. Therefore, we might have missed subtle but functionally significant metabolite differences between groups, a possibility that cannot be disconfirmed. From this perspective, the ratio of HVA to 5-HIAA may represent a larger order of change that is more likely to be detected than either metabolite individually.

Fourth, some researchers consider the commonly reported substantial positive correlation between HVA and 5-HIAA (replicated in our study) to be a function of a common metabolite transport mechanism. Ågren et al. (19), however, presented convincing evidence against this interpretation.

Our findings regarding the ratio of HVA to 5-HIAA are consistent with those of Risby et al. (20), who reported that the ratio was a far more sensitive indicator of antidepressant medication effect than either of its components, independent of diagnosis. Thus, we may speculate that the ratio of HVA to 5-HIAA may be a more sensitive indicator of biological perturbation—be it structural or pharmacological—than either system independently.

Assuming for purposes of argument that the ratio finding can be replicated and is not a consequence of methodological factors, we are confronted with its meaning. Based in part on the work of Ågren et al. (19), Risby et al. (20) suggested that the ratio of HVA to 5-HIAA may serve as a simple model of the functional interaction between the dopaminergic and serotonergic systems, with 5-HIAA unidirectionally driving HVA.

All of the groups in this study exhibited the expected high and positive correlation between HVA and 5-HIAA. This may be interpreted as evidence of the normality of the basic relationship between the dopaminergic and serotonergic systems, in contrast to their presumed dysregulation, reflected in the low correlations between HVA and 5-HIAA sometimes reported in depression (21).

The failure to find significant group differences in mean VBR has been reported by others (22–25), and many studies have failed to find significant differences in absolute concentrations of CSF HVA between schizophrenic patients and comparison subjects (26). More troublesome, at first glance, is our failure to find a significant negative correlation between VBR and CSF HVA. Pickar and Breier (27) pointed out that CSF HVA was more closely linked in their studies to pre-

TABLE 4. Correlations Between Lateral Ventricle-Brain Ratio (VBR), CSF HVA and 5-HIAA Concentrations, and Ratio of CSF HVA to 5-HIAA in Subjects With and Without Psychiatric Diagnoses

Item	Correlation (r)			
	VBR	HVA	5-HIAA	HVA: 5-HIAA
Patients with schizop- hrenia (N=45)				
VBR ^a		−0.22	0.15	−0.45 ^b
HVA ^c			0.70 ^b	0.59 ^b
5-HIAA ^c				−0.09
HVA:5-HIAA ratio ^c				
Patients with affective disorders (N=28)				
VBR ^d		0.01	0.17	−0.32
HVA ^e			0.81 ^f	0.49 ^f
5-HIAA ^e				−0.10
HVA:5-HIAA ^e				
Normal comparison subjects (N=91)				
VBR ^g		−0.24	−0.17	−0.12
HVA ^h			0.74 ^b	0.45 ^b
5-HIAA ^h				−0.23 ^b
HVA:5-HIAA ^h				

^adf=21.

^bp≤0.005.

^cdf=43.

^ddf=17.

^edf=26.

^fp≤0.01.

^gdf=66.

^hdf=92.

frontal cortical atrophy ($r=-0.54$) than to either generalized cortical atrophy ($r=-0.18$) or VBR ($r=0.08$), a finding at least partially consistent with ours. We shall explore this possibility in further analyses.

Finally, although we failed to find that premorbid competence (operationalized by number of years of education) had an effect on the relationship between VBR and CSF measures, it is possible that differences in negative symptoms in the patients with schizophrenia could have hidden a relationship between CSF HVA concentration and VBR or could have muted the finding regarding the relationship between VBR and the ratio of HVA to 5-HIAA. On the basis of our preliminary analyses, we do not think this is the case, but we will be reporting a detailed examination of clinical status, VBR, and CSF measures, especially among our psychiatrically “healthy” normal comparison group, in a later article.

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Panic Disorder and Suicidal Ideation and Behavior: Discrepant Findings in Psychiatric Outpatients

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***Objective:** Previous investigators found that persons who had ever met criteria for panic disorder or panic attacks reported more lifetime suicide attempts and ideation than persons who had ever met criteria for other psychiatric disorders. To determine whether outpatients with current panic disorders also report such differences, this study examined the suicide attempt rates, levels of suicidal ideation, and levels of hopelessness among four groups of psychiatric outpatients. **Method:** Structured clinical interviews were used to assign diagnoses to 900 consecutive psychiatric outpatients. These patients were administered the Scale for Suicide Ideation and the Beck Hopelessness Scale and were also questioned in detail about previous suicide attempts and past and present suicidal ideation. **Results:** None (0.0%) of the 73 patients with primary panic disorder without agoraphobia reported having made suicide attempts during their lifetimes. One (1.3%) of the 78 patients who had panic disorder with agoraphobia, 34 (7.0%) of the 485 patients who had mood disorders, and four (1.5%) of the 264 patients who had other psychiatric disorders reported suicide attempts. The mean scores on the Scale for Suicide Ideation and the Beck Hopelessness Scale of the patients with panic disorders and other disorders were significantly lower than the mean scores of the patients with mood disorders. **Conclusions:** The rates of suicidal ideation and behavior for psychiatric outpatients who had panic disorders were discrepant with those reported by the earlier group of investigators for a random community sample of persons who reported ever having had panic attacks or met criteria for panic disorders.*

(Am J Psychiatry 1991; 148:1195-1199)

Although mood and schizophrenic disorders are the diagnoses most frequently associated with eventual suicide, suicide attempts, and suicidal ideation (1), Weissman et al. (2) reported that persons who had ever met criteria for either panic disorder or panic attacks may be at greater risk for suicidal behavior. Of 18,011 persons who participated in the National Institute of Mental Health Epidemiologic Catchment Area study (3), Weissman et al. (2) identified 254 adults who were

diagnosed according to the National Institute of Mental Health Diagnostic Interview Schedule (4) as ever having met the criteria for a panic disorder. Their study group also included 667 individuals who met the criteria for panic attacks but not panic disorder and 4,857 who met the criteria for other psychiatric disorders. The persons with histories of panic disorder and panic attacks reported more suicide attempts and ideation than those with other psychiatric disorders. The suicide attempt rates were 20% and 12% for persons with panic disorder and panic attacks, respectively; the rate was 6% for persons with other psychiatric disorders. Furthermore, the higher suicide attempt rates and levels of suicidal ideation in the persons with panic disorder or panic attacks were not related to the coexistence of other psychiatric disorders, such as major depression, alcoholism, and drug abuse. Since Weissman et al. studied a random sample of adults in a community survey and based their diagnoses upon whether a person had ever met criteria for a disorder during his or her lifetime, it is unclear whether their findings would apply to patients currently having panic disorder and presenting for treatment in a clinical setting.

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Supported in part by the Foundation for Cognitive Therapy and Research, by grants from the American Suicide Foundation, NIMH, and the Norwegian Research Council for Science and the Humanities, and by contributions from Jack and Anita Saltz.

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The findings by Weissman et al. (2) run counter to the conventional wisdom as well as to the results of other studies regarding the relation of suicidal ideation and behavior to diagnosis. Persons diagnosed as having mood disorders according to *DSM-III-R* would be expected to describe more suicide attempts and ideation than patients with other kinds of disorders, since suicidal ideation and behavior are criteria used in establishing the presence of a mood disorder. Recently, Petronis et al. (5) analyzed retrospective and prospective data from the same set of Epidemiologic Catchment Area study data that Weissman et al. used. They found that the risk of a suicide attempt during 1 year before or after evaluation was associated with major depression, alcoholism, cocaine abuse, and marital disruption. They did not report panic disorder as a risk factor. Furthermore, retrospective studies of suicides have pointed to the diagnosis of depression as the antecedent or causal factor in the overwhelming majority of cases (1, 6). Persons with depressive disorders would be expected to report more suicide attempts and ideation than those with panic disorder or attacks. There is evidence that 26.7% of patients with panic disorder may develop major depression (7), and Fawcett et al. (8) have reported that panic attacks and a variety of other psychiatric symptoms in patients who have *primary diagnoses of major affective disorders* are related to eventual suicide.

The suicide rate for patients with panic disorder without depression, diagnosed in a clinical setting, has not yet been reported. Several follow-up studies of persons with anxiety states in general (not panic disorder) found suicide rates well above those seen in the general population (9, 10). However, studies among persons with anxiety states occur late in follow-up, and it is possible that these suicides are due to secondary depression or alcohol or substance abuse.

The question of which diagnostic group is at the highest risk for suicide is obviously of more than academic interest. High-risk groups need to be identified in any program for suicide prevention. Furthermore, there is evidence that the belief of patients with panic disorder that they are at high risk for suicide can unnecessarily alarm them and even exacerbate their symptoms (11, 12). Such a belief has already been fostered by headlines such as "Panic Can Be a Suicide Omen" (13).

The purpose of the present study was to compare the suicide attempt rates, levels of suicidal ideation, and levels of hopelessness reported by outpatients presenting with current primary panic disorders (without depression), mood disorders, and other disorders. Hopelessness was included along with suicide attempts and suicidal ideation because research studies have consistently found that hopelessness is a predictor of ultimate suicide (14–17). It is important to emphasize that the present study was not a replication of the procedure of Weissman et al. (2) but, rather, a description of the prevalence of suicidal ideation and behavior in psychiatric outpatients with panic disorders as compared to those with other types of psychiatric disorders.

METHOD

The subjects were 900 consecutive outpatients who were given diagnoses of *DSM-III* or *DSM-III-R* disorders at the Center for Cognitive Therapy between 1985 and 1989. Using prerelease versions of the eventual Structured Clinical Interview for *DSM-III-R* (SCID) (18), clinicians gave the majority of the patients diagnoses according to *DSM-III-R* criteria. The 1985 evaluations used the Structured Clinical Interview for *DSM-III* (SCID) (19). A study of the reliabilities of these SCID-derived diagnoses was reported by Riskind et al. (20) for a group of 36 outpatients several months before the present study began, and the interjudge agreements for both mood and anxiety disorders were greater than 80% for all of the raters. These same raters participated in the present study and trained subsequent raters who were used in later years.

The study group consisted of 504 women (56.0%) and 396 men (44.0%). Their mean \pm SD age was 36.65 \pm 11.47 years. The racial composition of the group was 868 (96.4%) white and 32 (3.6%) black. There were 73 patients (8.1%) who had panic disorder without agoraphobia, 78 (8.7%) who had panic disorder with agoraphobia, 485 (53.9%) who had mood disorders, and 264 (29.3%) who had other psychiatric disorders.

Of the 485 patients with primary mood disorders, there were 100 (20.6%) with single-episode major depression, 209 (43.1%) with recurrent-episode major depression, 41 (8.5%) with bipolar disorder, 88 (18.1%) with dysthymic disorder, 11 (2.3%) with cyclothymic disorder, 10 (2.1%) with atypical disorders, and 26 (5.4%) with depression not otherwise specified.

The majority (N=186, 70.5%) of the 264 outpatients with other primary psychiatric diagnoses had anxiety disorders. There were 84 (31.8%) with generalized anxiety, 41 (15.5%) with social phobia, 21 (8.0%) with obsessive-compulsive disorder, 14 (5.3%) with simple phobia, four (1.5%) with agoraphobia without panic attacks, 20 (7.6%) with atypical anxiety, and two (0.8%) with posttraumatic disorder. The diagnosis of primary alcohol abuse was given to five (1.9%) of the patients and the diagnosis of primary drug abuse to another five. Adjustment disorders were diagnosed for 42 (15.9%) of the patients, and 26 (9.8%) received other diagnoses that were not mood disorders.

After signing voluntary consent forms, the patients were routinely administered a standard intake battery of psychological tests and psychiatric rating scales that is given to all patients who are evaluated at the center. The SCID-derived diagnoses were made at this time, along with ratings on the Scale for Suicide Ideation (21) and the Beck Hopelessness Scale (22, 23) by experienced diagnosticians with doctoral-level degrees. Clinical interviews, which lasted 2 1/2 to 4 hours, included detailed questioning regarding previous suicide attempts and past and present suicidal ideation.

The Scale for Suicide Ideation is a 19-item rating scale used by a clinician in a structured interview to evaluate the intensity of a patient's specific attitudes, behavior,

TABLE 1. Suicide Attempts and Scores on the Scale for Suicide Ideation and the Beck Hopelessness Scale of 900 Patients With Psychiatric Disorders

Disorder	Patients Who Made Suicide Attempts		Score on Scale for Suicide Ideation ^a		Score on Beck Hopelessness Scale ^b	
	N	(%)	Mean	SD	Mean	SD
Panic without agoraphobia (N=73)	0	0.0	0.52	1.92	8.19	5.74
Panic with agoraphobia (N=78)	1	1.3	0.65	1.86	8.45	5.40
Mood (N=485)	34	7.0	2.29	4.85	11.60	4.90
Other (N=264)	4	1.5	0.67	2.24	8.17	5.21

^aRange of possible scores=0–38.^bRange of possible scores=0–20.

and plans with respect to committing suicide. Each item is rated on a 3-point scale ranging from 0 to 2. The ratings are summed to yield a total score, which may range from 0 to 38. Beck et al. (21) reported that the internal consistency of the scale was 0.89 for 90 subjects with suicidal ideation, and its interjudge reliability was 0.83. Ranieri et al. (24) have reported findings to support both the construct validity and the concurrent validity of the scale.

The Beck Hopelessness Scale consists of 20 true-false statements that assess the extent of pessimism about the future. This instrument showed a high degree of sensitivity in predicting eventual suicides in inpatient (14) and outpatient (15) samples. The coefficient alphas reported for the Beck Hopelessness Scale across diverse clinical and nonclinical populations are typically in the 0.80s, and its correlations with clinical ratings of hopelessness are in the 0.70s.

RESULTS

Table 1 shows the numbers of patients in the different diagnostic categories who had made suicide attempts during their lifetimes and their mean scores on the Scale for Suicide Ideation and the Beck Hopelessness Scale. Clinical examination revealed that none of the patients with the diagnosis of panic disorder without agoraphobia acknowledged ever having attempted suicide, and only one of the patients with the diagnosis of panic disorder with agoraphobia reported having made a suicide attempt. The odds ratio for patients with panic disorders having attempted suicide was only 0.12 (95% confidence interval=0.02–0.85). However, 34 (7.0%) of the 485 patients with mood disorders had made previous suicide attempts (table 1). The odds for patients with primary mood disorders having attempted suicide were 6.18 times those for patients with any other type of psychiatric disorder, including panic disorder (95% confidence interval=2.28–18.16).

To determine whether sex, race, and age should be controlled for in comparing the diagnostic groups' scores on the Suicide Ideation Scale, the correlations of sex (0=female, 1=male), race (0=white, 1=other), and age (years) with the scale scores were calculated. Because the scores were so positively skewed, square-root transformations were applied to the scores before we

conducted any statistical tests. The correlations with the Scale for Suicide Ideation scores were 0.01, 0.02, and –0.10 for sex, race, and age, respectively. Only the correlation with age was significant ($t=3.01$, $df=898$, $p<0.01$, two-tailed test). Therefore, age was used as a covariate. Controlling for age in a one-way analysis of covariance (ANCOVA), we found that the main effect for type of disorder was significant ($F=18.90$, $df=3$, 895 , $p<0.001$), and post hoc comparisons made with the Scheffé test indicated that the mean scores of the patients with panic disorders and the patients with other disorders were significantly lower than the mean score of the patients with mood disorders ($p<0.001$); the mean score for panic disorder patients was comparable to that of the patients with other disorders.

Again, to determine whether sex, race, and age should be controlled for in comparing the diagnostic groups' scores on the Beck Hopelessness Scale, the correlations of sex (0=female, 1=male), race (0=white, 1=other), and age (years) with the scores were calculated. The correlations were –0.03, –0.05, and 0.02 for sex, race, and age, respectively; none of the correlations was significant. Therefore, none of these demographic characteristics was controlled for. The one-way analysis of variance for the Beck Hopelessness Scale scores showed a significant difference according to type of disorder ($F=32.62$, $df=3$, 896 , $p<0.001$), and post hoc comparisons made with the Scheffé test found that the mean scores of the patients with panic disorders and the patients with other disorders were significantly lower than the mean score of the patients with mood disorders ($p<0.001$); there was no difference between the mean scores of the panic disorder patients and the patients with other disorders.

DISCUSSION

Our findings in a large group of psychiatric outpatients are inconsistent with the high rates of attempted suicide and levels of suicidal ideation found in a community survey by Weissman et al. of persons who had ever met criteria for panic disorder (2), but they support the positive relation between a patient's having active major depression and making a suicide attempt 1 year before or after baseline collection of data, as described by Petronis et al. (5). Only one (0.7%) of the 151 pa-

tients given the diagnosis of current panic disorder in the present study reported a previous suicide attempt, as compared to 20% of the respondents in the study by Weissman et al. who had had panic disorder at some time. In the present study, the current levels of suicidal ideation described by the patients currently experiencing panic disorder were significantly *lower* than those described by patients with mood disorders. This finding was based on the levels of suicidal ideation elicited by clinical examination of outpatients during their evaluations for treatment, whereas the interviewers in the study by Weissman et al. assessed suicidal ideation by asking respondents to indicate whether they had *ever* thought about death, felt as though they wanted to die, or thought about committing suicide at any time during their lifetimes.

Several theories may be advanced to account for the discrepancies between our findings and those reported by Weissman et al. (2). First, the epidemiological method used in their study may limit the generalizability of their findings to patients presenting for treatment. In their random sample of adults, diagnoses were based on whether a person had ever met criteria for a disorder during his or her lifetime. Therefore, the subjects selected by Weissman et al. may have differed systematically from those currently having panic disorders and seeking treatment. Depressed patients seeking treatment may be more severely ill than those in a community sample, and thus they would be more likely to describe a higher degree of suicidal ideation. On the other hand, patients with panic disorders who seek treatment may feel less hopeless about recovering and, therefore, be less likely to consider suicide than those who do not seek treatment.

Furthermore, the findings of Weissman et al. might reflect biased recall of information by their subjects. Panic attacks are very discrete, distressing events that patients can readily remember (25). Because lifetime diagnoses were used by Weissman et al., subjects who might have met criteria for both panic disorder and major depressive disorders several years previously may have been more likely to recall and emphasize the panic attacks and thus receive a diagnosis of a panic disorder. Therefore, the presence of a comorbid depressive disorder might have been missed. Moreover, the different interview techniques used by experienced clinicians examining clinic patients may yield different clinical and diagnostic data from those obtained by lay interviewers in a community survey.

The salient question is, What group of individuals is at the highest risk for ultimately committing suicide? This question was addressed by Barraclough et al. (6) in an exhaustive retrospective study of 100 consecutive suicides that focused on data obtained from medical records and/or from family interviews shortly after the suicides had occurred. The authors found that only seven of the 100 individuals who committed suicide had reported having had panic attacks at some time before their suicides. Moreover, panic attacks ranked 35th in frequency among patients who subsequently commit-

ted suicide, whereas all of the symptoms of depression had higher frequencies than did panic attacks. Depression, on the other hand, was a major determinant of suicide. In fact, 70% of the 93 subjects diagnosed as mentally ill received the diagnosis of depression. The findings from that study suggest that panic attacks per se were a negligible risk factor. However, the recent report by Fawcett et al. (8) suggests that panic attacks and other clinical phenomena such as anxiety, anhedonia, and alcoholism in patients selected on the basis of their diagnoses of major depressive disorders are associated with greater risk of suicide within a year.

Another source of information for determining the relation between panic and suicidal ideation and behavior is the diagnoses of patients at the time that they were examined following a nonfatal suicide attempt. A recent study by Sakinofsky et al. (26) reported the diagnoses of patients evaluated at a general hospital shortly after they attempted suicide. The diagnoses were distributed across five disorders, none of which was panic disorder.

Finally, it should be noted that we would expect the findings of Weissman et al. (2) to appear in a more concentrated form in our study, since our subjects were presumably sicker than those in a community study. As pointed out by Berkson (27), patients admitted to medical centers are likely to show an enhanced association between two clinical variables (such as panic and suicide) as compared to individuals in a community survey. Contrary to this expectation, the association reported by Weissman et al. did not appear at all in our clinical group.

It is possible that the findings of Weissman et al. were an artifact resulting from the joint attachment of another variable to two unrelated variables. For example, cocaine abuse was found to be a predictor of suicide attempts in the Epidemiological Catchment Area data set analyzed by Petronis et al. (5) in terms of suicide attempts reported within 1 year before or after the diagnostic interview. (Their time frame differed from that used by Weissman et al., who analyzed the data in terms of reports of *lifetime* suicide attempts and ideation relevant to death.) Since cocaine abuse frequently produces panic attacks and is a determinant of suicide attempts, it may be the interlocking variable joining panic and suicidal ideation and behavior.

The present study, taken together with previous studies of suicidal behavior, does not support the conclusion that panic in itself constitutes a risk factor for suicide. Analysis of the diagnoses of patients who committed suicide does not indicate that panic disorder preceded the fatal suicide attempts. Analysis of the diagnoses of patients who made nonfatal suicide attempts similarly failed to show such an association. The present study, which examined panic patients at the height of their panic disorder, failed to show any significant previous suicide attempts or any of the indices that would suggest increased risk of suicide in the future. In the context of previous studies of suicide and attempted suicide, the findings reported by Weiss-

man et al. (2) should be viewed as anomalous, warranting further exploration.

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Mass Hysteria Among Student Performers: Social Relationship as a Symptom Predictor

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***Objective:** In April 1989 an outbreak of illness suddenly afflicted student performers in Santa Monica, Calif., and an extensive investigation revealed no environmental cause. To clarify the details of the epidemic and determine whether mass hysteria occurred, the authors examined physical, psychological, and social factors that might have contributed to the outbreak. **Method:** Participating middle- and high-school performers were surveyed; 93% (N=519) responded; cases were defined as students who had one or more symptoms during the outbreak. A stepwise logistic regression analysis was used to determine significant predictors of illness. **Results:** Characteristic features of mass hysteria were present, including preponderance of illness in girls, symptom transmission by sight or sound, presence of hyperventilation, and evidence of psychological or physical stress. Symptomatic and asymptomatic groups differed in frequency of several physical and psychological variables, but observing a friend become sick was the best predictor of the development of symptoms. **Conclusions:** These results confirm earlier research demonstrating multiple psychological and physical factors that contribute to such outbreaks, particularly symptom transmission through social networks. Investigators should explore social transmission as an additional characteristic feature of mass hysteria in order to facilitate early identification of future outbreaks.*

(Am J Psychiatry 1991; 148:1200-1205)

Despite increasing sophistication and technological advances in epidemiological and environmental sciences, outbreaks of mass hysteria continue to perplex investigators. Most occur suddenly in a heightened emotional climate, and growing concerns about pollution escalate anxiety about possible toxic causes. School and health officials face the difficult task of carrying out a thorough but hurried investigation, given the time constraints posed by the possibility of a potentially lethal, undetected toxin or contaminant.

Although environmental deterioration is a real concern that will increase and shape epidemics of sudden onset, investigating psychological and social factors can

be critical to early identification and management. When psychosocial features predominate, the epidemic is considered mass hysteria, defined as the group occurrence of a constellation of physical symptoms that suggest an organic cause but result from a psychological one (1). Typical features that help differentiate psychogenic outbreaks of illness from those due to physical causes include the absence of laboratory test results and physical findings that confirm a specific organic cause; a preponderance of illness in girls or women; the apparent transmission of illness by sight or sound or both; no illness among another group sharing the environment; the presence of hyperventilation or syncope; a preponderance of illness in adolescents or preadolescents; benign morbidity, often with rapid spread, followed by rapid remission of symptoms; illness relapses in the setting of the original outbreak; and evidence of unusual physical or psychological stress (2, 3).

Even with knowledge of these features, investigators have difficulty differentiating psychogenic epidemics from those resulting from physical causes. For example, two outbreaks of epidemic neuromyasthenia reported in the 1950s (4, 5) continued to be debated over a decade later, when McEvedy and Beard (6) argued for a psychological rather than an infectious cause. Moreover, such outbreaks are not infrequent. The precise

Presented at the 143rd annual meeting of the American Psychiatric Association, New York, May 12-17, 1990. Received Sept. 21, 1990; revision received Feb. 8, 1991; accepted March 20, 1991. From the Department of Psychiatry and Biobehavioral Sciences, UCLA School of Medicine, and the West Los Angeles VA Medical Center. Address reprint requests to Dr. Small, UCLA Neuropsychiatric Institute, 760 Westwood Plaza, Los Angeles, CA 90024.

The authors thank Bradley W. Warren, M.D., for his help in developing and distributing the questionnaires, Shirley Fannin, M.D., for encouraging and facilitating the study, Eugene Tucker, Ph.D., for his cooperation and support, and Lynn A. Fairbanks, Ph.D., for statistical consultation.

The views expressed are those of the authors and not necessarily those of the Department of Veterans Affairs.

prevalence of mass hysteria is unknown, but a pilot study of Quebec schools found an estimated rate of one outbreak per 1,000 school settings per year (7). In this country, our research group learns of one to two outbreaks resembling hysteria each year.

In a previous report (2), we described the characteristic features of mass hysteria in an outbreak of illness among school chorus members, in which environmental contamination was a critical concern. In this report, we describe a similar but larger outbreak and ask the following questions: 1) Were characteristic features of mass hysteria present? 2) What psychological and physical factors may have contributed to the epidemic? 3) Did symptoms spread through social networks?

THE EPIDEMIC

On April 13, 1989, approximately 2,000 spectators and 600 student performers assembled in Santa Monica, Calif., Civic Auditorium for the 40th annual "Stairway-of-the-Stars" concert. The recital was the major classical performance of the year for these 6th through 12th graders from three local schools. Soon after the assembly began at 7:30 p.m., complaints of physical illness interrupted the performance. Headache, dizziness, weakness, abdominal pain, and nausea spread swiftly among the students. The soprano girls appeared most severely affected, and 16 of them fainted. Eventually 247 students became ill, and by 9:20 p.m. officials were forced to evacuate the auditorium; this was one of the largest emergency evacuations in Santa Monica history.

The fire department dispatched two paramedic squad units, two engines, and a truck and set up a treatment control station on the auditorium lawn. Some students remained calm, but many of the younger girls were frightened and tearful as they observed rows of schoolmates lined up on stretchers. Eight ambulances rushed the 19 most severely ill students to five local hospitals, where results of physical examinations and screening laboratory tests revealed no abnormalities. Earlier in the day at the concert rehearsal, two girls had complained of dizziness, nausea, and faintness. Some students had smelled fresh paint, and fans had been placed to improve ventilation. After the evening outbreak, firefighters searched extensively for the suspected environmental toxin but were unable to detect toxic fumes or other contaminants.

The following day school officials announced that evidence of fumes or toxic materials was never found and that they would proceed with the scheduled second concert that night. Some paramedics and firefighters had suspected mass hysteria during the course of the outbreak. Parents, however, were unconvinced, and many kept their children at home. Rumors about the outbreak's cause spread through the community and ranged from "insufficient oxygen" to "mass hysteria in the air." Although many parents believed that toxic fumes caused the illness, characteristic features of mass hysteria were apparent.

METHOD

We first heard about the epidemic from a radio report during the evacuation of the concert. Having investigated similar outbreaks of illness among schoolchildren (G.W.S.), our research team offered its services to the local board of health and school district. Officials from both the Los Angeles County Department of Health Services and the Santa Monica-Malibu Unified School District accepted this offer, and one of us (M.W.P.) served as a primary liaison.

Student performers came from one high school (grades 9 through 12) and two middle schools (grades 6 through 8) within the district to comprise a band, an orchestra, and a chorus. Approximately 40 elementary-school honor students also performed but were not included in the study. On the basis of our prior experience with similar outbreaks, we developed a one-page questionnaire to ascertain additional information about physical and psychosocial aspects of the outbreak. School officials then distributed the questionnaires to all middle- and senior-high school student performers, who filled them out during class several weeks after the outbreak. An estimated 560 middle- and senior-high school students performed at the concert, so the approximate response rate for those at risk was 93% ($N=519$; 339 girls and 180 boys). Because incomplete responses were eliminated, denominators for some analyses were less than the total of 519. The study was conducted in accordance with the University of California, Los Angeles, Human Subjects Protection Committee; individual responses were kept anonymous. Data were also collected from interviews with parents, public health and school officials, and attending physicians.

Cases, identified from the questionnaires, were defined as children having one or more symptoms during the outbreak. In addition, we measured the severity of illness by the number of symptoms. Children whose illness was graded as severe had more than three symptoms or a hospital visit, those whose illness was graded as moderate had two or three symptoms, and those whose illness was graded as mild had only one symptom. Pearson chi-square statistics were used to determine statistical differences among independent and dependent variables of interest. Two-tailed tests were applied and $df=1$ unless otherwise specified. To determine which variables contributed to the illness, a stepwise logistic regression analysis, which allows for both continuous and categorical variables, was performed.

RESULTS

The overall rate of illness was 48% ($N=247$). The most common symptoms included headache, dizziness, weakness, abdominal pain, and nausea (table 1). The 19 hospitalized children were more likely to experience symptoms of longer duration (more than 1 hour) than were the 228 nonhospitalized symptomatic children (84% [$N=16$] versus 51% [$N=102$]; $\chi^2=7.38$, $p<0.01$).

TABLE 1. Symptoms Reported by 519 Student Performers Involved in an Outbreak of Illness Characteristic of Mass Hysteria

Symptom	Boys (N=180)		Girls (N=339)		Total	
	N	%	N	%	N	%
Headache	43	23.9	100	29.5	143	27.6
Dizziness ^a	16	8.9	67	19.8	83	16.0
Weakness ^b	12	6.7	43	12.7	55	10.6
Abdominal pain	13	7.2	36	10.6	49	9.4
Nausea	15	8.3	31	9.1	46	8.9
Shortness of breath	10	5.6	35	10.3	45	8.7
Chills ^c	8	4.4	33	9.7	41	7.9
Shaking	9	5.0	30	8.8	39	7.5
Chest pain	8	4.4	14	4.1	22	4.2
Cough	8	4.4	13	3.8	21	4.0
Fainting ^d	1	0.5	16	4.7	17	3.3
Numbness	3	1.7	10	2.9	13	2.5
Tingling	1	0.5	12	3.5	13	2.5
Wheezing	3	1.7	8	2.4	11	2.1
Inability to open eyes	3	1.7	5	1.5	8	1.5
Loss of voice	2	1.1	4	1.2	6	1.2
Vomiting	1	0.5	5	1.5	6	1.2
Other	9	5.0	17	5.0	26	5.0

^aSignificant difference between sexes ($\chi^2=9.56$, $df=1$, $p<0.005$).

^b $\chi^2=3.88$, $df=1$, $p<0.05$.

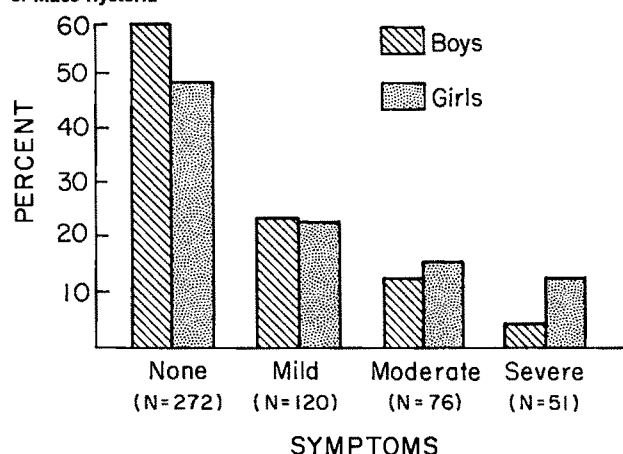
^c $\chi^2=3.84$, $df=1$, $p<0.05$.

^d $\chi^2=6.44$, $df=1$, $p<0.05$.

Chronic medical illness (usually asthma and other respiratory problems) was also more common in the hospitalized symptomatic children than in the nonhospitalized symptomatic and the asymptomatic children (58% [N=11] versus 22% [N=47] versus 9% [N=18]; $\chi^2=32.03$, $df=2$, $p<0.0005$).

The rate of illness for girls was higher than that for boys (51% [N=174] versus 41% [N=73]; $\chi^2=5.05$, $p<0.02$), and girls were more likely than boys to experience severe symptoms (figure 1). Symptom patterns, moreover, differed between the sexes (table 1); girls were significantly more likely than boys to experience dizziness, weakness, and chills. Girls were also more likely to experience faintness than were boys (4.7% [N=16] versus 0.5% [N=1]; $\chi^2=6.44$, $p<0.05$); 16 of the 17 children who reported faintness were girls.

Student performers were members of a chorus, band, or orchestra from each of the participating district schools. Rates of illness according to school and performance group membership revealed that chorus members, particularly those from one of the middle schools, were most likely to develop symptoms (Pearson $\chi^2=78.9$, $df=8$, $p<0.0001$). Fifteen of the 17 children who fainted were chorus members. The rate of illness according to grade level demonstrated a trend toward a preponderance of illness among the younger students (grade 6=58.9% [N=43], grade 7=54.9% [N=62], grade 8=45.0% [N=27], grade 9=46.8% [N=36], grade 10=38.6% [N=17], grade 11=41.3% [N=26], and grade 12=37.7% [N=23]; $\chi^2=11.14$, $df=6$, $p<0.09$). Those students who sang in the soprano chorus section were more likely to experience moderate or severe symptoms than were children who sang in the other chorus sections ($\chi^2=7.54$, $p<0.006$). Moreover,

FIGURE 1. Sex-Specific Rates of Illness, According to Severity of Illness, Among 519 Student Performers Involved in an Outbreak Characteristic of Mass Hysteria^a

^aGirls were more likely to experience severe symptoms than were boys ($\chi^2=11.39$, $df=3$, $p<0.01$).

59% (N=10) of the children who fainted were chorus sopranos. There were no significant differences in rates of illness among band and orchestra sections or among wind instrument sections and other sections.

Symptomatic and asymptomatic children differed according to a variety of physical and psychological variables. The group of symptomatic children had a higher frequency of both chronic medical illness (25% [N=59] versus 10% [N=22]; $\chi^2=16.65$, $p<0.00005$) and recent acute illness (17% [N=40] versus 11% [N=25]; $\chi^2=3.94$, $p<0.05$). Symptomatic children were also less likely to have reported an "A" grade point average than were asymptomatic ones (41% [N=96] versus 54% [N=141]; $\chi^2=8.61$, $p<0.005$) but were more likely to have experienced the death of a close relative or friend (70% [N=164] versus 55% [N=147]; $\chi^2=10.42$, $p<0.005$).

Symptomatic children were more likely to observe friends becoming sick than were asymptomatic children. Seventy-one percent (N=170) of the symptomatic children, compared to only 45% (N=114) of asymptomatic ones, reported observing a symptomatic friend ($\chi^2=35.76$, $p<0.00005$). Of the 17 children who fainted, 14 (82%) reported observing a friend develop symptoms.

Because so many physical and psychological variables appeared to contribute to the outbreak, we performed a stepwise logistic regression analysis to determine which variables best predicted symptoms (table 2). The dependent variable was the presence of symptoms. This analysis revealed that observing a friend become sick was the best predictor of the development of symptoms. Several other variables also contributed significantly, particularly chronic medical illness and age. Number of days absent from school during the past month and presence of acute physical illness were not significant predictors in the regression analysis.

The final survey question asked respondents to describe what they thought had caused the illness. These

TABLE 2. Stepwise Logistic Regression Analysis to Determine Which Variables Best Predicted Symptoms in 473^a Student Performers Involved in an Outbreak of Illness Characteristic of Mass Hysteria

Step	Variable	df	Log Likelihood	Improvement		Goodness of Fit	
				χ^2	p	χ^2	p
1	Observed sick friend	1	-305.053	44.07	0.000	280.60	0.000
2	Chronic illness	1	-294.724	20.66	0.000	259.94	0.002
3	Age	1	-288.607	12.23	0.000	247.71	0.006
4	Reported grade point average	1	-284.498	8.22	0.004	239.49	0.02
5	Previous grief	1	-281.146	6.70	0.01	232.78	0.03
6	Sex	1	-278.858	4.58	0.03	228.21	0.04

^aOnly 473 of the 519 subjects were included because of missing data in 46 cases.

responses were then divided into two groups that described either physical causes (e.g., paint fumes, insect spray) or psychological causes (e.g., stress, anxiety). Compared to the other children, the group of children who attributed the outbreak to a physical cause had a higher frequency of chorus membership (53% [N=170] versus 27% [N=26]; $\chi^2=19.55$, $p<0.0005$) and hospitalization (100% [N=17] versus 0%; $\chi^2=4.93$, $p<0.02$), as well as a different symptom cluster, including a higher rate of headaches (35% [N=114] versus 12% [N=12]; $\chi^2=19.05$, $p<0.0005$) and dizziness (20% [N=66] versus 9% [N=9]; $\chi^2=6.50$, $p<0.01$). Children who observed symptomatic friends were significantly more likely to attribute a physical cause to the outbreak than were other children (61% [N=197] versus 38% [N=37]; $\chi^2=14.62$, $p<0.0001$).

DISCUSSION

Characteristic Features of Mass Hysteria

We found the characteristic features of mass hysteria in the Santa Monica epidemic (2, 3). Although paint fumes or another undetected toxin might have existed before the use of fans and might have contributed to the illness, extensive environmental searches revealed no specific organic cause. The symptoms were transient, relatively benign, and not present among the audience of nonperformers who shared the environment. Afflicted children experienced typical symptoms, including hyperventilation (i.e., shortness of breath, tingling, numbness). In fact, the five most common symptoms of the Santa Monica outbreak (table 1) were identical to those reported in the Templeton, Mass., epidemic nearly a decade earlier (2). Not only did we find a higher rate of illness among girls, but also more severe symptoms and a difference between the sexes in symptom clusters (table 1).

Contributing Physical and Psychological Factors

Both physical and psychological variables differed in the symptomatic and asymptomatic groups, and the stepwise logistic regression analysis confirmed that several factors contributed to this outbreak. The higher rate of chronic medical illness among symptomatic chil-

dren could indicate that previous long-term experience with physical illness and "patient status" heightens a child's psychological susceptibility to hysterical symptoms. In line with this explanation, McEvedy and Beard (8) reported that symptomatic persons had higher rates of sick leave, poorer overall health, and more frequent hospitalizations before an epidemic afflicting hospital personnel. May and associates (9) also noted an increase in "sickness experience or behavior" before an outbreak of benign myalgic encephalomyelitis in a girls' school: symptomatic students had attended the school sick bay more often than asymptomatic ones during the prior year. An alternative explanation for the differences in rates of chronic medical illness in the present study is that physical disability (e.g., respiratory insufficiency from asthma) itself contributes to sensitivity to physical stress (e.g., singing) during the performance. The presence of acute illness in some of the Santa Monica students may have contributed through this latter mechanism. Previous studies have identified several forms of contributing physical stress, including playing wind instruments (10) and prolonged standing and singing (2). Another possibility is that chronic illnesses, such as asthma, increased a child's sensitivity to undetected toxins (e.g., paint fumes).

Symptomatic children reported having lower grade point averages than did asymptomatic children. Few investigators have recorded academic achievement following these epidemics. Knight and associates (11) reported no significant differences in mean IQ between symptomatic and asymptomatic schoolchildren. Following an outbreak of hysteria among young women, Johnson (12) found that symptomatic persons were less likely to have completed high school than were asymptomatic ones. In the present study, actual grade point averages were not available, and our finding may reflect the students' willingness to reveal their abilities or their self-perceived educational achievement or both, rather than actual achievements.

We found that the symptomatic group of children had a higher frequency of previous grief than did the asymptomatic group. This finding replicates our earlier study (1), which demonstrated higher rates of early loss (death within the family and parental divorce) in symptomatic children than in asymptomatic ones. In that study, the epidemic occurred in the context of several impending separations and losses for the children, and we hypothe-

sized that early loss predisposed children to anxiety about anticipated loss—thus the higher frequency of such losses among the symptomatic children. Impending loss did not seem to characterize the Santa Monica outbreak, although the psychological stress of performance anxiety probably contributed to symptoms.

How persons at risk understand the cause of these outbreaks may well affect the likelihood of the development of symptoms. Students who attributed a physical cause to the illness were more likely to have been chorus members, hospitalized, and observing a sick friend than were those who attributed a psychological cause. Moreover, the symptomatic children who were convinced of a physical cause demonstrated a different constellation of symptoms than did the other symptomatic children. Certain types of symptoms and symptom severity may contribute to the belief that the symptoms are “real” and not simply “in the mind.” Concerns about the environment have been important aspects of other epidemics (2, 13, 14). Several of the Santa Monica participants complained about the smell of paint in the auditorium, and although a guard rail had been painted recently, no toxic source was identified. Citizens of Santa Monica are known for their sensitivity and activism concerning the environment, and this attitude could have contributed to anxiety and the likelihood of attributing a physical cause to the illness.

Social Transmission of Symptoms

Rates of illness were higher and more severe symptoms were present in certain groups and subgroups of students. The illness preferentially struck chorus members from one of the middle schools, particularly girls in the soprano section. These students were in close proximity to one another so that symptom transmission through sight and sound would be facilitated, accounting for part of this pattern. However, the response to the question regarding observations of afflicted friends and the stepwise logistic regression analysis demonstrated the importance of social relationships in the spread of symptoms.

Results of the present study are consistent with earlier research over the past decade, pointing to social influences on these outbreaks. In previous Massachusetts epidemics, we noted that a social hierarchy, in which younger children “imitate” older ones, could explain the spread of symptoms (1) and that hospitalized children were more likely than nonhospitalized symptomatic children to have observed close friends becoming sick before their own symptoms developed (2). Other investigators have reported symptom transmission through social networks. Moss and McEvedy (15) found that symptoms spread along the social hierarchy from older to younger students in an outbreak of overbreathing among schoolgirls. Kerckhoff and associates (16) reported that symptomatic persons were twice as likely as asymptomatic ones to identify other symptomatic persons as their friends. Social spread of symptoms can be indirect, as found in a recent outbreak

among elementary-school students in Georgia. Philen and co-workers (3) described transmission of illness through both family and social networks, in which parents, and not the afflicted children, communicated to one another, thereby spreading symptoms “by proxy.” In the Santa Monica epidemic, children who observed friends become sick were more likely to attribute the outbreak to a physical cause than were other children; this may indicate a greater level of empathy and understanding when a student observes a friend believed to be physically ill.

Methodological Considerations

Because data were collected 3 weeks after the epidemic, discussions among students, parents, teachers, and school officials could have influenced the results. Data for most previous studies of mass hysteria were collected after several weeks, and our conclusions may apply only to investigations performed after such a delay. Because some questionnaires were incomplete, only 82% of the responses could be used for some analyses. However, given the high estimated questionnaire response rate (93%), data were available for a relatively high proportion (at least 82% of 93%, or 76%) of the total population at risk.

Outbreaks of hysteria are difficult to study. Rapid response is essential, since most epidemics are short-lived. Many people in the community are reluctant to cooperate and may express concerns that suggestions of a psychological cause will stigmatize them as weak-minded or suggestible. People with such objections are often reassured when the psychiatric investigator emphasizes the importance of understanding the epidemic, establishing that the environment is safe, and learning how to prevent future outbreaks. Local health boards generally have a mandate to ensure public health safety, and developing a liaison with such agencies will facilitate access to subjects at risk.

CONCLUSIONS

Our investigation of the Santa Monica epidemic identified the characteristic features of mass hysteria described in similar epidemics. Several physical and psychological factors appeared to contribute to the epidemic. Although physical proximity may partly explain the clustering of cases among student groups, the best predictor of the development of symptoms was observing a friend with symptoms. We recommend that social transmission of symptoms be included as an additional characteristic feature of mass hysteria in order to facilitate early recognition of psychogenic outbreaks of illness.

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Long-Term Outcome of Antidepressant Treatment for Bulimia Nervosa

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Objective: The purpose of this study was 1) to replicate previous work indicating that antidepressant medication is superior to placebo in the treatment of bulimia nervosa and 2) to assess the long-term efficacy of this form of treatment. **Method:** Eighty patients entered a three-phase treatment protocol. An 8-week double-blind initiation phase was used to compare the effects of desipramine and placebo. Patients who responded satisfactorily to desipramine entered a 16-week maintenance phase. Patients who remained well were then randomly assigned to either desipramine or placebo for 6 additional months (discontinuation phase). The primary outcome measure was binge frequency, which was assessed weekly by self-report diaries. **Results:** In the initiation phase the superiority of desipramine over placebo in reducing binge frequency was demonstrated. Patients treated with desipramine had a mean reduction in binge frequency of 47% at termination, whereas patients taking placebo experienced a mean increase of 7%. Less than half of the patients treated with desipramine met the criteria for entering the maintenance phase, and 29% of the patients entering that phase relapsed in the following 4 months. There were not enough patients in the discontinuation phase to permit clear conclusions about the need for continued antidepressant medication after 6 months of treatment. **Conclusions:** The study documents a beneficial effect of desipramine in the treatment of bulimia nervosa when compared to placebo. However, limited improvement and considerable relapse with continued treatment suggest serious limitations to the long-term efficacy of a single antidepressant trial in treating bulimia nervosa.

(Am J Psychiatry 1991; 148:1206-1212)

In the last decade, 13 controlled studies (1-13) explored the usefulness of antidepressant medication in the treatment of bulimia nervosa, and all but two found the active medication to be superior to placebo. However, major questions concerning the use of antidepressant medication in this syndrome remain unanswered. In particular, the long-term efficacy of such treatment has not been fully investigated. The longest

of the published controlled trials examined the effectiveness of 16 weeks of drug treatment (6), but most trials lasted only 8 weeks. It remains unclear whether patients who respond to treatment experience additional improvement with continued medication and whether the response is sustained when medication is stopped. We therefore designed a three-phase study to assess the long-term efficacy of the tricyclic antidepressant desipramine in women of normal weight with bulimia nervosa.

The first phase was an 8-week, double-blind, placebo-controlled trial the purpose of which was to replicate previous studies that had found desipramine to be superior to placebo (4, 5, 7). To determine whether the benefits of antidepressant treatment persisted with continued medication, the patients who responded to desipramine entered a 16-week open maintenance phase. Finally, patients who sustained their improvement through the maintenance phase entered a double-blind, placebo-controlled discontinuation phase of 24 weeks. The purpose of this last phase was to establish whether 6 months of successful antidepressant treatment led to sustained improvement or whether there was substan-

Presented at the 29th annual meeting of the American College of Neuropsychopharmacology, San Juan, Puerto Rico, December 10-14, 1990. Received July 26, 1990; revision received Feb. 27, 1991; accepted March 18, 1991. From the Department of Psychiatry, College of Physicians and Surgeons, Columbia University. Address reprint requests to Dr. Walsh, Department of Psychiatry, College of Physicians and Surgeons, Columbia University, 722 West 168th St., Box 98, New York, NY 10032.

Supported in part by NIMH grant MH-38355. Desipramine and placebo were provided by Merrell Dow Pharmaceuticals, Inc., Cincinnati.

The authors thank Rena Appel, Catharine Buttinger, Janel Cariño, Thomas Cooper, Sondra Dantzic, Alexander Glassman, Jeffrey Halpern, David Lindy, Valerie Lukasik, Fay Stetner, Linda Wong, and Sally Woodring for assistance in conducting this study.

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tial relapse among patients whose medication was discontinued.

METHOD

To participate in this study, patients had to have met the *DSM-III-R* criteria for bulimia nervosa for at least 1 year. In addition, we included only women between the ages of 18 and 45 years whose weight was 85%–120% of their ideal body weight according to the 1959 Metropolitan Life Insurance Company tables. Patients were excluded if they 1) were suffering from acute or chronic medical conditions, 2) were judged to be acutely suicidal, 3) were currently being treated with psychotropic medication, 4) had abused drugs or alcohol in the past year, or 5) had had a previous adequate trial of antidepressant medication (a minimum of 200 mg/day of desipramine for at least 3 weeks or equivalent doses of other medications).

Patients were recruited through advertisements in the local news media publicizing the availability of free treatment for bulimia nervosa. Patients were also referred by therapists in the community. All patients were screened by telephone and by interview with a research assistant to establish their appropriateness for the study. During a second screening interview, each patient was seen by a project psychiatrist who obtained a complete medical and psychiatric history. At this visit the Structured Clinical Interview for *DSM-III-R* (14) was also conducted by a research assistant to determine *DSM-III-R* diagnoses. Informed consent was obtained from each patient entering the study after the treatment protocol had been fully explained by a project psychiatrist.

A total of 217 potential subjects had screening interviews for admission into the study. Ninety-eight of these entered the study; the remainder consisted of 56 patients who did not meet entry criteria, 46 who were not interested in the treatment being offered, and 17 who expressed interest in the treatment but failed to return after the evaluation interviews.

Initiation Phase

Patients were first entered into a 2-week, single-blind, placebo washout phase. If, after these 2 weeks, patients had reduced their weekly binge frequency by 75% or more or were binge eating less than twice a week, they were not assigned to a treatment. Ten patients met these criteria for placebo response, and eight additional patients dropped out during this phase of the study. The remaining 80 patients were randomly assigned to desipramine treatment or placebo for a 6-week double-blind trial.

Double-blind trial. Of the 80 patients entering the double-blind phase, 39 were assigned to the placebo group and 41 were assigned to the desipramine group. Two patients (one from each group) failed to return after assignment to treatment and are not included in the data analyses.

During the first week after randomization, the dose was gradually raised to 200 mg/day of desipramine (four 50-mg tablets) or the equivalent dose of placebo. If tolerated, this dose was continued for 3 weeks. Four weeks after randomization, patients who continued to binge eat had their dose raised to 300 mg/day of desipramine or the equivalent dose of placebo and continued to take this dose until the end of the initiation phase. Blood samples were obtained at weeks 5 and 6 and at termination (if this occurred at other than week 5 or 6) to determine plasma desipramine concentrations. These samples were collected to monitor compliance with the treatment regimen and to determine whether adequate blood levels were achieved by the patients treated with desipramine.

Patients were seen once a week by project psychiatrists. The psychiatrists were instructed to inquire about the patients' general health, eating behavior, level of mood disturbance, and side effects and to offer approval when symptoms improved. Sessions lasted no more than 30 minutes and did not constitute either in-depth psychological therapy or a structured cognitive-behavioral approach.

Patients were asked to record the number of daily binge-eating and purging episodes in a diary that was submitted at each visit. In addition, each week the treating psychiatrist completed the Hamilton Rating Scale for Depression (15) and a physician's clinical global impression scale. A battery of self-report questionnaires was completed at the time the patients were assigned to treatment and again at termination: the Eating Attitudes Test (16), the Beck Depression Inventory (17), the Body Shape Questionnaire (18), the SCL-90 (19), the Social Adjustment Scale (20), the State-Trait Anxiety Inventory (21), and the Rosenberg Self-Esteem Scale (22). Each patient was weighed weekly.

In addition to the self-report questionnaires and diaries obtained at each visit, semistructured interviews were conducted at randomization and at termination by an independent rater blind to treatment assignment and self-report measures.

Open trial. After the 6-week double-blind initiation phase, patients who had been randomly assigned to the placebo group and had not improved were offered an open trial of desipramine. As in the double-blind phase, patients were seen once a week for 6 weeks, and a similar dosing schedule was used.

Maintenance Phase

To enter the maintenance phase, patients were required to have achieved a reduction of 50% or more in binge frequency in the last 2 weeks of the initiation phase compared to baseline (i.e., the average binge frequency during the 2 weeks before they started the active medication). Patients who met this criterion while being treated with desipramine during either the double-blind or the open initiation phase were continued openly on a regimen of desipramine for 16 weeks. During the maintenance phase, patients were seen twice a month,

TABLE 1. Clinical Characteristics of Patients With Bulimia Nervosa Before and After Treatment With Placebo (N=38) or Desipramine (N=40)^a

Variable	Before Treatment				After Treatment				ANCOVA		
	Placebo Group		Desipramine Group		Placebo Group		Desipramine Group		F	df	p
Age (years)	25.7	5.6	24.8	4.5							
Height (in)	65.0	2.7	65.4	2.1							
Weight (lb)	132.4	17.8	136.2	16.1	135.4	18.8	134.2	15.1	13.4	1, 65	0.001
Body mass index (kg/m ²)	22.0	2.3	22.4	1.9	22.3	2.5	22.0	1.9	12.6	1, 65	0.001
Duration of illness (years)	6.6	4.5	6.7	3.6							
Binge episodes per week	8.3	5.4	8.1	4.6	8.6	7.2	4.3	3.9	14.2	1, 72	<0.001
Vomiting episodes per week	13.0	16.7	10.8	12.7	13.3	17.5	7.8	14.4	5.5	1, 72	0.02
Eating Attitudes Test score	39.6	15.2	39.8	16.9	37.7	15.1	29.9	16.0	5.1	1, 62	0.03
Body Shape Questionnaire score	135.3	28.3	148.7	35.6	120.5	34.2	101.6	36.6	6.4	1, 48	0.02
Hamilton depression scale score	7.3	4.6	8.3	4.6	6.5	5.1	6.0	4.7	1.5	1, 72	n.s.
Beck Depression Inventory score ^b	15.0	11.1	10.4	7.3	13.0	11.0	9.2	7.7	0.4	1, 69	n.s.
SCL-90 scores											
Global symptom index	2.1	0.7	1.9	0.5	2.0	0.7	1.6	0.4	7.3	1, 63	0.009
Anxiety scale	2.0	0.8	1.9	0.6	1.9	0.8	1.7	0.6	1.9	1, 64	n.s.
Depression scale	2.5	1.0	2.3	0.8	2.5	0.9	1.9	0.7	7.8	1, 64	0.007
Somatization scale	1.7	0.8	1.7	0.5	1.7	0.7	1.7	0.5	0.6	1, 64	n.s.
Obsessive-compulsive scale	2.2	1.0	2.0	0.7	2.1	1.0	1.6	0.6	9.3	1, 64	0.003
Interpersonal sensitivity scale	2.5	1.1	2.3	0.8	2.3	1.0	2.0	0.7	2.6	1, 64	n.s.
Psychoticism scale	1.8	0.7	1.6	0.5	1.8	0.7	1.4	0.4	9.3	1, 64	0.003
Paranoid ideation scale	1.8	0.8	1.6	0.6	1.7	0.7	1.4	0.5	3.7	1, 64	0.06
Hostility scale	1.9	0.9	1.7	0.8	1.9	1.0	1.4	0.6	5.8	1, 64	0.02
Phobic anxiety scale	1.5	0.7	1.5	0.5	1.5	0.8	1.4	0.4	0.8	1, 64	n.s.
State-Trait Anxiety Inventory scores											
State	51.5	14.3	48.1	12.2	49.3	14.3	45.5	12.4	0.5	1, 71	n.s.
Trait	54.3	10.3	51.9	10.5	54.1	11.6	46.5	10.2	7.1	1, 60	0.01
Social Adjustment Scale score	2.2	0.4	2.3	0.5	2.1	0.6	2.0	0.4	0.9	1, 47	n.s.

^aSample sizes vary for some measures because of missing data.^bSignificant difference between groups before treatment ($t=2.13$, $df=62$, $p=0.04$).

and plasma desipramine levels were ascertained monthly. Patients were considered to have relapsed if, for 2 consecutive weeks, they binged at more than 50% of their baseline binge frequency.

Discontinuation Phase

Patients who did not relapse during the maintenance phase were offered participation in the double-blind discontinuation phase. In this phase, patients were randomly assigned either to continue taking the same dose of desipramine they had received during the maintenance phase or to switch to placebo. Patients assigned to placebo had their medication tapered from desipra-

mine to placebo over a period of 2 weeks. Patients in the discontinuation phase were seen twice a month for 6 months. The same definition of relapse was used in this phase as in the maintenance phase.

Data Analysis

Clinical characteristics of the desipramine and placebo groups assessed during the evaluation period were compared by using Student's *t* test (two-tailed). Intent-to-treat analyses were completed using termination assessment data from both the patients who completed the 6-week initiation phase and the patients who discontinued before week 6. For patients who did not

complete a full 6 weeks of taking drug or placebo, data from the last visit were carried forward.

The major outcome measure analyzed for the initiation phase was the number of binge episodes per week. Binge frequency data were not normally distributed; therefore, log transformations of binge episodes per week were used to approximate a normal distribution. To assess the influence of medication assignment and of depression on treatment response, a two-way analysis of covariance (ANCOVA) was performed, with drug assignment (desipramine versus placebo) and depression (present versus absent) as independent variables and baseline binge frequency as the covariate. Depression was judged present or absent by the clinician at the time of random assignment to treatment. Patients meeting criteria for current major depression, dysthymia, or depressive disorder not otherwise specified were assigned to the depressed group in order to ensure that the nondepressed group would be relatively free of depressive symptoms. The frequencies of remission, defined as no binge episodes in the week before termination, were compared in the two groups by using the chi-square statistic. One-way ANCOVAs with drug assignment as the independent variable were completed for various symptom measures (e.g., frequency of vomiting and scores on the Beck Depression Inventory, the Eating Attitudes Test, the Body Shape Questionnaire, and the SCL-90), with baseline values on these measures as the covariate.

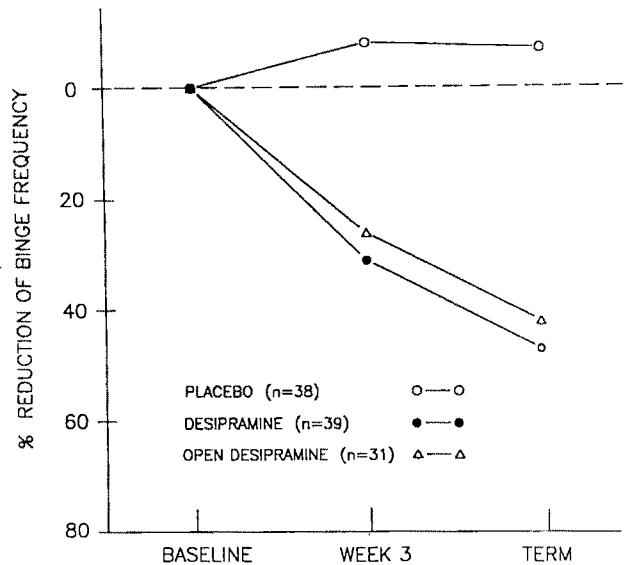
To determine whether pretreatment levels of symptoms predicted treatment outcome, we compared baseline clinical characteristics of patients whose binge frequencies declined by 50% or more ("responders") to those of patients with a lesser degree of improvement ("nonresponders") during initial treatment with desipramine or placebo. Student's *t* test (two-tailed) was used to evaluate continuous variables, and the chi-square test was used for categorical variables.

RESULTS

Initiation Phase

Double-blind trial. Of the 78 patients who were randomly assigned to a treatment group and returned for at least one visit after the assignment, 40 were assigned to desipramine and 38 to placebo. Baseline clinical characteristics of these 78 patients are summarized in table 1. There were no significant differences between the two groups on any of the baseline measures except the Beck Depression Inventory; patients assigned to placebo had a significantly higher mean±SD Beck inventory score than patients assigned to desipramine (15.0 ± 11.1 and 10.4 ± 7.3 , respectively). Eighteen (23.1%) of the total sample had histories of anorexia nervosa, and 40 (51.3%) were diagnosed as currently depressed (i.e., had major depression, dysthymia, or depressive disorder not otherwise specified) at the time of evaluation. There was no significant difference between

FIGURE 1. Binge Frequency (Expressed as Percent Reduction of Baseline Binge Frequency) of Patients With Bulimia Nervosa During Double-Blind and Open Initiation Phases of Desipramine or Placebo Treatment^a



^aBinge frequency at termination (TERM) was calculated from eating diaries completed in the last 2 weeks before termination. For patients not completing a full 6-week trial of drug or placebo, data from the last visit to the project psychiatrist were carried forward. Information on binge frequency at termination was not available for one patient in the desipramine group, so data from only 39 of the 40 patients in that group are presented.

the mean±SD binge frequencies of the depressed and nondepressed groups at the time of random assignment (depressed patients, 9.1 ± 5.6 binges per week; nondepressed patients, 7.2 ± 4.2 binges per week; $t = -1.61$, $df = 76$, $p = 0.11$). A small proportion (5.1%, $N = 4$) of the patients in the study used laxatives, not vomiting, as their primary method of purging.

Fifteen patients failed to complete the full 6-week initiation phase. In the placebo group, two were lost to follow-up, one relocated temporarily, one became pregnant, one was discontinued by her treating physician because of cocaine abuse, and one requested early discontinuation because of lack of improvement. In the desipramine group, three were lost to follow-up, one relocated temporarily, and five experienced intolerable side effects. Thus, 63 patients completed the full 6-week double-blind initiation phase: 31 of the 40 in the desipramine group and 32 of the 38 in the placebo group.

There was a significant difference in reduction of binge frequency between the two groups (figure 1 and table 1). Patients treated with desipramine had a mean reduction in binge frequency of 47% at termination, whereas patients taking placebo experienced a mean increase of 7%. The two-way ANCOVA with baseline binge frequency as the covariate showed a significant effect of medication for weeks 4 through termination (at termination, $F = 9.76$, $df = 1, 72$, $p < 0.003$). Neither the effect of depression nor the interaction between drug and depression was significant. The remission rate was 12.5% (five of 40) for the desipramine group and

7.9% (three of 38) for the placebo group ($\chi^2=0.45$, $df=1$, $p=0.50$).

The median plasma desipramine level of patients receiving active medication at termination was 272 ng/ml (range=52–1463 ng/ml). Patients assigned to the desipramine group were taking significantly fewer tablets per day (mean \pm SD=5.1 \pm 1.2) than patients assigned to placebo (5.6 \pm 0.8) ($t=2.29$, $df=63$, $p=0.03$).

ANCOVAs of the following measures showed a significant effect of drug assignment: frequency of vomiting and scores on the Eating Attitudes Test, the Body Shape Questionnaire, the SCL-90 (global symptom index and the depression, obsessive-compulsive, psychoticism, and hostility subscales), and the anxiety trait scale (table 1). There was also a significant medication effect on weight at termination; patients taking desipramine had an average decrease in weight of 2.0 lb, whereas patients treated with placebo had an average increase in weight of 2.9 lb. Similarly, there was a significant effect of drug assignment on body mass index (the patient's weight in kilograms divided by the square of her height in meters). Although the changes in body mass index were relatively small, the placebo group experienced a mean increase, whereas the group treated with desipramine had a mean decrease, resulting in a significant group effect. There was a significant difference between the desipramine and placebo groups in clinical global improvement at termination, as assessed by the independent rater (mean \pm SD=2.75 \pm 1.2 and 3.41 \pm 1.1, respectively; $t=2.19$, $df=55$, $p=0.03$).

Of the measures of symptoms listed in table 1, only duration of bulimia nervosa and pretreatment Body Shape Questionnaire score were significantly related to outcome during the double-blind initiation phase. Patients who were at least 50% improved at termination had a longer mean duration of illness ($t=2.35$, $df=74$, $p=0.02$) and a higher mean score on the Body Shape Questionnaire ($t=2.33$, $df=58$, $p=0.02$). In addition, there was a trend for responders to have a lower mean number of pretreatment vomiting episodes per week ($t=-1.74$, $df=69$, $p=0.09$). There was no significant relation between treatment outcome and history of anorexia nervosa, presence of laxative abuse, age, lowest reported adult body mass index, binge frequency, and scores on the Eating Attitudes Test, the Hamilton Rating Scale for Depression, the Beck Depression Inventory, the SCL-90, the State-Trait Anxiety Inventory, the Social Adjustment Scale, and the Rosenberg Self-Esteem Scale.

Open trial. Thirty-one patients entered the 6-week open trial of desipramine. Four patients were discontinued because of intolerable side effects experienced within the first 2 weeks of treatment, and two patients were lost to follow-up after 2 weeks. Binge frequency response for patients entering the open trial is summarized in figure 1. There was an average decrease in binge frequency of 42% at termination, a value comparable to the results from the double-blind phase. Three (9.7%) of the patients were in remission at termination.

Maintenance Phase

A total of 29 patients from the double-blind and open initiation phases met the criteria for entering the maintenance phase. Eight of the 29 did not enter the maintenance phase because of lack of interest, intolerance of side effects, or other problems (e.g., alcohol abuse). Thus, 21 patients entered the maintenance phase.

Eleven (52.4%) of the patients completed the 16-week continuation of desipramine, six (28.6%) relapsed, two (9.5%) developed intolerable side effects, and two (9.5%) were lost to follow-up. Patients who completed the full 16 weeks of the maintenance phase did not show statistically significant improvement during this phase; mean \pm SD weekly binge frequency at entry was 1.9 \pm 1.4 and at the end of the maintenance phase was 1.0 \pm 1.4 (paired t test, $t=1.50$, $df=10$, $p=0.17$). Plasma desipramine levels of 16 patients were available during the maintenance phase; the mean \pm SD level was 311 \pm 153 ng/ml.

Discontinuation Phase

Nine of the 11 patients who completed the maintenance phase agreed to enter the double-blind discontinuation phase of the study. Five patients were randomly assigned to continue taking desipramine and four were assigned to placebo. Of the patients taking desipramine, four (80%) completed the full 24-week trial and one relapsed 3 weeks after assignment of treatment. Two of the four patients assigned to placebo relapsed within 7 weeks of assignment, while the remaining two continued to do well. One of these patients completed the full 24 weeks, and the other had completed 13 weeks when she discontinued treatment with us.

Other Antidepressant Treatment

Fifteen patients who failed to respond adequately or who relapsed while taking desipramine were treated openly with a monoamine oxidase inhibitor (MAOI) ($N=10$) or fluoxetine ($N=5$). After an average of 10 weeks of treatment, 13 of these patients had a mean reduction of binge frequency of 67% and three were in remission. Two patients did not complete an adequate trial of medication (one had not responded after 3 weeks of phenelzine treatment and was hospitalized for further care, and the other was lost to follow-up after 3 weeks).

DISCUSSION

This study confirmed previous investigations in demonstrating that desipramine was superior to placebo in the short-term treatment of bulimia nervosa. Both the mean decline in binge frequency (47%) and the remission rate (12.5%) during the initiation phase of this trial were comparable to those reported in other con-

trolled trials of antidepressants in bulimia (1–13). We also confirmed previous findings (4, 6, 9) that response to antidepressant treatment was not related to the pretreatment presence of depression.

Compared to placebo treatment, the use of desipramine was also associated with significant reductions in other measures of behavioral and psychological disturbances characteristic of bulimia nervosa, such as frequency of vomiting and Eating Attitudes Test and Body Shape Questionnaire scores. Significant effects of medication were also observed on several other measures of psychopathology: the trait scale of the State-Trait Anxiety Inventory and the SCL-90 global symptom index and four subscales. However, drug effects were not observed on other measures of anxiety and depression, possibly because of the relatively low pretreatment scores on these instruments.

As in other studies, patients' weights changed little during short-term medication treatment. However, an ANCOVA using pretreatment weight as a covariate demonstrated a significant reduction of weight in patients receiving desipramine compared to those receiving placebo. One possible explanation of this phenomenon is that patients who respond to medication reduce the amount of calories consumed in binge episodes without increasing their intake of nonpurged calories (23). It is of interest that the weight loss associated with desipramine treatment contradicts the popular notion that tricyclic antidepressant therapy for bulimia results in weight gain.

Although we examined the ability of a number of pretreatment characteristics to predict short-term outcome, only baseline score on the Body Shape Questionnaire and duration of illness were significantly associated with outcome. In both instances, the results obtained suggest a relation between symptom measure and outcome that runs counter to clinical expectation. Patients with greater concern for body shape and weight at evaluation were more likely to improve in treatment, and longer duration of illness was also associated with a more favorable treatment response. Because these findings were noted on the basis of post hoc analyses, the value of these characteristics as predictors of treatment outcome should not be viewed as established until the results are replicated.

While the current study clearly documents a beneficial effect of desipramine in the treatment of bulimia nervosa, it also points to shortcomings in the use of desipramine as the sole method of treatment for this illness. At the end of the initiation phase, patients receiving desipramine continued to binge 4.3 times weekly, on average, despite a 47% mean reduction from baseline binge frequency. The data from the maintenance and discontinuation phases demonstrate serious limitations to the long-term efficacy of a single tricyclic antidepressant as the sole method of treatment. Less than half of the patients treated with desipramine met the criteria for entering the maintenance phase, and 29% of the patients who entered the maintenance phase relapsed in the following 4 months. This relapse rate is

identical to that recently reported by Pyle et al. (24) for patients maintained on imipramine treatment for 6 months following initial treatment. In the current study, the low rate of initial response to desipramine coupled with the significant rate of relapse resulted in a flow of patients into the discontinuation phase that was too small to permit drawing a clear conclusion about the need for continued antidepressant medication after 6 months. The limited data available suggest that it may not be possible to discontinue medication successfully even after 6 months of sustained improvement.

The findings of this study, therefore, raise questions about the role of antidepressant medication in the treatment of bulimia nervosa. We found that the use of a single antidepressant medication was frequently an insufficient treatment for this illness. Other investigators have reported that patients who fail to respond to a single antidepressant trial may not be refractory to all antidepressant therapy (24–26). Thirteen patients from the current study experienced a mean reduction of binge frequency of 67% when treated with an MAOI or fluoxetine after an unsuccessful trial of desipramine. These results are consistent with controlled trials of MAOIs and fluoxetine in treating bulimia nervosa (9, 10, 13) and suggest that additional trials of medication should be considered for patients who fail to respond adequately to an initial course of treatment with an antidepressant.

Reports of impressive and sustained benefits of cognitive-behavioral forms of psychotherapy also challenge the status of antidepressant medication as a primary mode of treatment for bulimia nervosa (27, 28). A study recently reported by Mitchell et al. (12) compared imipramine to intensive group psychotherapy in which cognitive-behavioral techniques were used. Both group psychotherapy alone and group psychotherapy combined with imipramine produced a substantially greater reduction in binge frequency than imipramine alone. While that study represents a major advance over previous work, there are limitations to its generalizability. The group psychotherapy was unusually intensive, entailing from two to five 3-hour sessions per week for 6 weeks. It is unclear whether less intensive forms of psychotherapy are equally effective. Therefore, in the absence of additional studies directly comparing pharmacological and nonpharmacological interventions, we believe it is premature to conclude that the latter are uniformly superior. For example, before a definitive conclusion regarding the superiority of cognitive-behavioral psychotherapy can be reached, it may be important to compare the efficacy of this form of treatment with pharmacological strategies that incorporate sequential medication trials.

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Buspirone: Sedative or Stimulant Effect?

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Objective: The primary objectives of this study were to evaluate the effects of initial and continued administration of buspirone on sleep induction and maintenance and sleep stage parameters, to determine the presence or absence of any drug-induced side effects, and to ascertain the presence or absence of sleep disturbances following abrupt withdrawal of the drug. **Method:** Six insomniac subjects who had chronic complaints of difficulty falling asleep and/or staying asleep and who were in good physical health, were not suffering from any major mental disorders, and had not used any medication for at least the last month participated in a 16-night sleep laboratory protocol. The protocol consisted of 4 placebo-baseline nights, 7 nights on which buspirone, 10 mg at bedtime, was administered, and 5 placebo-withdrawal nights. **Results:** Wake time after sleep onset increased moderately during the first 3 nights of drug administration (there was a marked and significant increase on the first night) and increased by lesser degrees with continued drug administration. Overall, reports of side effects were infrequent. Following drug termination, there was a delayed and mild increase in sleep difficulty above baseline. **Conclusions:** These data not only confirm that buspirone lacks sedative effects but also suggest that the drug may have stimulant properties. Further, these findings suggest that buspirone has limited usefulness in anxious patients with concomitant sleep difficulties.

(Am J Psychiatry 1991; 148:1213-1217)

Buspirone is an antianxiety agent with a molecular formula of 8-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-dione monohydrochloride. Its chemical structure and clinical pharmacology are uniquely different from the other anxiolytic agents, including benzodiazepines and barbiturates (1). Buspirone does not bind to benzodiazepine receptors or directly or indirectly to γ -aminobutyric acid receptors (2, 3). It appears to have a strong affinity for dopamine receptors and for serotonin type 1 receptors located primarily in the hippocampus (3). Also, buspirone differs from other anxiolytics in that it lacks the anticonvulsant action, muscle relaxant effects, and sedative properties typical of benzodiazepines (1).

Because anxiety occurs in many medical and psychiatric disorders, an anxiolytic drug that is effective but does not impair psychomotor and cognitive functioning is highly desirable. Studies of healthy volunteers which

have assessed buspirone's effects on psychomotor functioning, eye-hand coordination, and reactive skills, including simulated driving, have shown that impairments, if present, are less severe than those following equivalent doses of diazepam and tend to improve with continued administration of the drug (4-7). Also, when combined with alcohol, buspirone, in contrast to benzodiazepines, does not produce an additive effect in terms of impairing psychomotor functioning (8, 9).

Use of buspirone has not been shown to lead to either abuse (2, 10, 11) or physical and psychological dependence (1, 12, 13). In addition, the investigators in one study (14) reported that patients treated for 6 months with buspirone did not show significant rebound anxiety or withdrawal symptoms (15, 16) when rapidly switched to placebo. However, one report (13) suggested that buspirone may not be entirely free of the potential for dependence.

Buspirone has been associated with adverse effects such as headache, nervousness, dizziness, lightheadedness, and, to a lesser degree, drowsiness, weakness, nausea, and insomnia (17, 18). The presence and severity of drug-induced insomnia is of particular importance, since the majority of patients who use anxiolytics suffer also from sleep disturbances. Thus, the primary objectives of this study were to evaluate the effects on sleep of initial and continued administration of 10 mg

Presented in part at the 143rd annual meeting of the American Psychiatric Association, New York, May 12-17, 1990. Received Aug. 7, 1990; revision received Jan. 25, 1991; accepted Feb. 15, 1991. From the Sleep Research and Treatment Center and the Department of Psychiatry, Pennsylvania State University College of Medicine. Address reprint requests to Dr. Manfredi, Department of Psychiatry, Pennsylvania State University College of Medicine, 500 University Drive, Hershey, PA 17033.

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TABLE 1. Effects of 10 mg of Buspirone on Sleep Induction and Maintenance in Six Insomniac Subjects

Variable	Baseline (nights 2-4)		Drug Administration				Withdrawal			
			Nights 5-7		Nights 9-11		Nights 12-14		Nights 15-16	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Sleep latency (min)	22.0	14.9	22.3	16.0	21.7	10.2	16.4	9.5	19.3	8.3
Wake time after sleep onset (min)	35.4	13.5	49.3	37.3	45.0	45.6	37.9	30.4	45.4	45.0
Total wake time (min)	57.4	18.8	71.6	34.1	66.7	41.4	54.3	32.9	64.7	42.0
Sleep time (%)	88.0	3.9	85.1	7.1	86.1	8.6	88.7	6.9	86.5	8.8
Number of awakenings	7.0	3.1	6.7	2.6	6.6	4.0	6.7	3.2	7.2	3.5
Wake time (%)										
First third of night	4.7	1.8	6.8	6.5	5.5	3.9	4.4	3.3	4.1	3.1
Second third of night	6.5	4.0	8.5	2.0	4.3	2.4	8.5	10.0	6.4	5.4
Third third of night	12.1	4.9	16.8	23.9	19.5	26.7	11.7	7.9	19.0	24.0

of buspirone at bedtime to insomniac subjects, to determine the presence or absence of any drug-induced side effects, and to ascertain the presence or absence of sleep disturbances following abrupt withdrawal of the drug.

METHOD

Six insomniac subjects (four women and two men), 26-61 years of age (mean±SD=41.7±15.7 years), were selected to participate in the study. The subjects were in good physical health and had not used any medication for at least the past month. The subjects demonstrated mild degrees of anxiety and depression but did not have mental disorders (for example, psychoses or major affective disorders) that would require psychopharmacologic treatment or that would prevent them from adhering to the study guidelines and requirements. Each subject had at least a 6-month history of difficulty falling asleep, staying asleep, or both. To qualify for the study, subjects had to report a history of taking an estimated 30 minutes to fall asleep and/or obtaining fewer than 6.5 hours of total sleep time. Throughout the study the subjects were instructed not to nap, not to alter their level of daily activity significantly, and not to use any medication. Each subject was fully informed of the nature of the experiment, gave his or her written consent, and was paid for participation in the study.

The experimental protocol included 16 consecutive nights, which were divided into 4 placebo-baseline nights followed by 7 nights of drug administration and 5 placebo-withdrawal nights. The first placebo-baseline night allowed for adaptation to the new sleeping environment, and nights 2-4 were used to obtain baseline measurements. Buspirone's effects on sleep efficiency variables and on sleep stages were evaluated during nights 5-11. The effects of drug withdrawal were determined on nights 12-16, when matching placebo was again administered.

On each night of the study, the subjects were continuously monitored for 8 hours by EEG, electromyogram, and electro-oculogram. Subsequently, all sleep recordings were scored according to standardized criteria (19). Variables assessed from the sleep recordings in-

cluded sleep induction (sleep latency), sleep maintenance (wake time after sleep onset), sleep induction and sleep maintenance (total wake time), and percentage of sleep time. We also assessed sleep stage variables (including REM sleep and stages 1-4), number of REM periods, interval from sleep onset to the first REM period (REM latency), and percentage of slow wave (stages 3 and 4) sleep. In addition, the distribution of wakefulness and sleep throughout the night was examined by thirds of the night. Thirds of the night were established by subtracting sleep latency from the total amount of laboratory time (480 minutes) and then dividing the remaining time into equal thirds.

Throughout the study, upon awakening in the morning, the subjects completed a questionnaire on which they estimated the time it had taken to fall asleep, the number of awakenings during the night, total sleep time, the soundness and quality of sleep, and morning sleepiness. They also completed an adjective checklist that used a 9-point scale for assessing tension, anxiety, and other mood factors. Tension and anxiety were also assessed on a separate 7-point scale and on a 10-cm analog scale that ranged from "extremely calm" to "extremely agitated."

Each night before going to sleep, the subjects completed a questionnaire in which they estimated their sleepiness and tension/anxiety during the day and their degree of sleepiness at bedtime. They also rated their presleep levels of anxiety on the 10-cm analog scale and the State section of the State-Trait Anxiety Inventory (20).

Side effects on each of the 16 nights of the study were recorded from information on the questionnaires completed by the subjects each morning and evening and from subjects' spontaneous reports of side effects to laboratory personnel. In addition, when the subjects returned home after completion of the withdrawal period, they were instructed to call if they had any subsequent adverse effects or difficulties.

Data Analysis

All of the sleep records were scored according to standardized criteria (19) independent of any knowledge of the experimental conditions. In order to correct

TABLE 2. Effects of 10 mg of Buspirone on Sleep Stage Variables in Six Insomniac Subjects

Variable	Baseline (nights 2-4)		Drug Administration				Withdrawal			
			Nights 5-7		Nights 9-11		Nights 12-14		Nights 15-16	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Sleep time (%)										
REM	24.2	3.7	21.3	3.3	23.5	4.7	26.3	3.9	25.9	7.2
Stage 1	5.2	1.1	6.6	3.0	6.5	1.2	6.4	2.0	5.5	1.5
Stage 2	67.6	3.9	69.5	4.4	67.7	5.6	63.9	4.8	65.8	6.8
Stage 3	2.9	2.7	2.6	2.1	2.3	2.2	3.4	3.8	2.8	2.3
Stage 4	0.1	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Slow wave	3.0	2.7	2.6	2.0	2.3	2.2	3.4	3.8	2.8	2.3
REM sleep time (%)										
First third of night	16.6	7.9	8.0 ^a	5.4	10.3 ^b	6.2	17.3	4.9	17.3	6.3
Second third of night	23.2	7.3	26.3	5.3	25.8	4.1	29.8	8.9	26.8	9.1
Third third of night	32.8	4.0	28.4	7.8	36.5	9.4	32.3	4.7	33.8	11.9
REM latency (min)	81.2	18.0	104.8	39.7	94.5	48.5	69.5	19.5	60.2	5.9
Number of REM periods	4.2	0.6	3.8	0.8	3.7	0.5	4.4	0.8	4.6	0.5
Length of REM period (min)	24.8	5.4	24.6	9.0	27.2	6.5	26.5	6.9	24.4	8.9
Total REM sleep (min)	102.6	16.7	86.6	13.7	97.7	22.7	112.5	21.1	109.4	37.1

^aSignificantly different from baseline ($t=4.71$, $df=70$, $p<0.01$).

^bSignificantly different from baseline ($t=2.87$, $df=70$, $p<0.05$).

for the number of comparisons, Dunn's multiple comparison two-tailed t test (21) was used to contrast the drug and withdrawal conditions with the baseline condition for each of the effectiveness and sleep stage variables. An experimentwise error estimate derived from a two-way analysis of variance (22) for each variable was based on the interaction between each subject and individual night of the study excluding night 1 ($df=70$). Within Dunn's multiple comparison test, the appropriate Scheffé weight adjusted this error estimate for the specific comparison made (21).

Comparisons of sleep efficiency and sleep stage variables were made between the baseline set of nights (nights 2-4) and each of the following sets of nights: initial drug administration (nights 5-7), continued drug administration (nights 9-11), short-term withdrawal (nights 12-14), and extended withdrawal (nights 15 and 16). In addition, a night-by-night analysis of the initial drug administration period and the entire drug withdrawal condition was completed by contrasting the values for sleep induction and sleep maintenance variables of each night with the corresponding mean values of the baseline condition. A probability value of $p<0.05$ was selected as the critical confidence level.

RESULTS

Effects on Sleep Induction and Sleep Maintenance

The effects of buspirone on sleep induction and sleep maintenance during drug administration and after withdrawal are reported in table 1. Wake time after sleep onset increased 95.2%, from 35.4 minutes at baseline to 69.1 minutes on the first drug night (night 5) ($t=2.70$, $df=70$, $p<0.05$). In addition, wake time after

sleep onset and total wake time increased moderately (39.3%, $t=1.57$, $df=70$, *n.s.*, and 24.7%, $t=1.38$, $df=70$, *n.s.*, respectively) during the first 3 nights of drug administration (nights 5-7).

During continued drug administration (nights 9-11), wake time after sleep onset increased 27.1% from baseline ($t=1.08$, $df=70$, *n.s.*), and total wake time increased 16.2% ($t=0.91$, $df=70$, *n.s.*).

During short-term drug withdrawal (nights 12-14), wake time after sleep onset and total wake time were similar to baseline values ($t=0.28$, $df=70$, *n.s.*, and $t=0.30$, $df=70$, *n.s.*, respectively). However, during extended drug withdrawal (nights 15-16), wake time after sleep onset increased slightly (28.2%) on both nights ($t=1.01$, $df=70$, *n.s.*).

Effects on Sleep Stage Variables

The effects of administering and withdrawing buspirone on sleep stages and related variables are shown in table 2. During initial drug administration (nights 5-7), REM latency increased from baseline ($t=1.66$, $df=70$, *n.s.*), and the total amount of REM sleep decreased ($t=1.88$, $df=70$, *n.s.*). Also, in the first third of the night for nights 5-7, the percentage of REM sleep decreased significantly from baseline, while in the remaining two-thirds of the night the percentage of REM sleep did not change significantly.

During continued drug administration (nights 9-11), the amounts of REM sleep and sleep in stages 1-4 were generally consistent with baseline values. However, REM latency continued to be greater than at baseline during those nights ($t=0.94$, $df=70$, *n.s.*), although to a lesser extent than during the initial 3 drug nights. Further, there was a significant decrease from baseline in the percentage of REM sleep in the first third of the night.

During the initial and extended withdrawal periods, there were no significant changes noted in the percentages of REM sleep and sleep in stages 1–4 compared to baseline.

Subjective Reports and Side Effects

The subjects estimated that their sleep was relatively undisturbed during both initial and continued drug administration compared to baseline. On nights 5–7, estimates of sleep latency and number of awakenings changed little from baseline. With continued use of buspirone, subjects estimated that the quality and soundness of sleep were also similar to baseline.

There were no significant changes noted in estimates of morning or daytime tension and anxiety during the drug administration period. One patient, however, did experience a mild increase in morning anxiety following the third night of drug administration.

After drug withdrawal, two patients estimated a mild increase in daytime and bedtime sleepiness during the early withdrawal period. Overall, reports of side effects were relatively infrequent. One patient complained of mild to moderate headaches, which occurred in the morning and evening during initial and continued drug administration as well as during withdrawal. This same patient also complained of diarrhea during early drug withdrawal. None of the patients reported difficulty in concentration, increased jitteriness, or any other physical complaints. Clinical follow-up of the subjects during the 2-week period after the sleep laboratory study revealed no nocturnal difficulties or daytime anxiety.

DISCUSSION

Our results demonstrate that buspirone, 10 mg at bedtime, can produce moderate degrees of sleep difficulty during initial drug administration. On the first night of drug administration, there was a marked and significant increase in wakefulness following sleep onset (95.2%), and for the first 3 drug nights, this value and total wake time were increased moderately. Similar sleep-disrupting effects have been described in the rat (23). In the current study, with continued administration of the drug over the 1-week drug period, this increase in wakefulness diminished, indicating development of some tolerance to the drug's sleep-disrupting effects. Also, following drug termination, there was a delayed and mild increase in sleep difficulty above baseline during the fourth and fifth withdrawal nights.

The effects of buspirone on sleep structure are also clearly different from those induced by benzodiazepines, which usually suppress slow wave sleep (stages 3 and 4) and increase stage 2 sleep (24). In contrast, in the present study, buspirone, 10 mg at bedtime, did not significantly affect slow wave or stage 2 sleep, which is in agreement with another report (25). However, the total amounts of REM sleep and REM latency were affected during initial drug administration, which is in agree-

ment with other reports (23, 25). REM latency was increased by almost 30%, and the amount of REM sleep during the first third of the night was significantly suppressed. However, with continued drug administration, the actual amount of REM sleep as well as REM latency tended to return to baseline levels, which again implies the development of tolerance to certain of the drug's effects.

Previous studies (15, 16) have shown that withdrawal of rapidly eliminated benzodiazepines, even after only relatively short periods of drug administration, is associated with various degrees of sleep disturbance, including rebound insomnia. In this study mild and delayed sleep disturbance did occur following withdrawal of buspirone. A previous study found temporary increases in symptoms of some anxious patients after withdrawal of buspirone (13). Those findings taken in conjunction with the data from this study indicate that withdrawal of buspirone produces mild and delayed withdrawal symptoms.

Given our small sample size, the possibility of a type II error needs to be considered. The consistent trend in all of the efficacy data suggests at least a mild stimulant property of the drug as well as mild withdrawal difficulties. If the power of the analysis were increased by increasing the sample size, one would expect even more of the differences between baseline and the drug conditions to be significant.

It has already been established that a major advantage of buspirone is its lack of daytime sedation (25–27). According to some investigators, this advantage favors buspirone over other anxiolytic compounds, for which daytime sleepiness is considered as one of the most disturbing adverse effects. However, while this study demonstrated that buspirone lacks sedative effects, it also suggests that the drug may have stimulating effects, as indicated by the moderate sleep disturbance associated with initial use and the mild sleep difficulty associated with continued use. Further, the lack of (28) or delay in achieving (29) a therapeutic anxiolytic effect with buspirone may be due more to this stimulating property than to lack of sedation or anxiolysis.

Other evidence suggests that buspirone may act as a stimulant. First, buspirone has been shown to increase the rate of firing of both dopaminergic and noradrenergic cells (3). It has also been shown to stimulate some autonomic functions, such as respiration (30, 31). Furthermore, cases of hypomania (32) and mania (33) as well as of panic and high blood pressure (34) with buspirone use have been described, and a certain potential role of the drug in the treatment of attention deficit disorder has been proposed (35). The drug's potential use as an antidepressant is being investigated, and there have been positive results (36, 37). It is possible that this "antidepressant" effect is related to buspirone's stimulating properties and to its triggering some cases of panic, hypomania, and mania. Finally, abnormal movements (38) such as oral dyskinesia (39) and generalized myoclonus (40) have been reported with administration of the drug.

Clinicians need to be aware of these findings when prescribing buspirone, in order to inform patients appropriately of possible initial and continued disruption of sleep and possible mild and delayed sleep disturbance following withdrawal. This information is particularly relevant for the many patients with anxiety who have associated insomnia. Thus, a major clinical implication of this study is that buspirone would be expected to have limited usefulness in anxious patients who have concomitant sleep difficulties.

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A Behavioral Approach to Achieving Initial Cocaine Abstinence

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Objective: The aim of this study was to assess the efficacy of a behavioral treatment program for achieving initial cocaine abstinence in individuals enrolled in outpatient treatment for cocaine dependence. **Method:** Thirteen consecutively admitted outpatients were offered behavioral treatment consisting of contingency management procedures and the community reinforcement approach. Fifteen consecutively admitted outpatients were offered treatment with 12-step counseling. All 13 of the patients who were offered the behavioral treatment accepted it; 12 of the patients offered 12-step counseling accepted it. **Results:** Eleven of the 13 patients in the behavioral treatment were retained for 12 weeks of treatment, compared with five of the 12 patients given 12-step counseling. Ten of the patients given behavioral therapy achieved 4 weeks of continuous cocaine abstinence, compared with only three of those given 12-step counseling. Six of the patients in the behavioral treatment group achieved 8 weeks, and three achieved 12 weeks; none of the patients in the 12-step counseling program achieved 8 weeks. **Conclusions:** The behavioral treatment described in this paper offers promise as an effective intervention for achieving initial cocaine abstinence. A randomized trial is underway to assess the generality of these findings.

(Am J Psychiatry 1991; 148:1218-1224)

At least 22 million individuals in the United States have tried cocaine, and 1-2 million are dependent (1-3). A subset (8% or more) of cocaine users administer it intravenously, and the likelihood of intravenous use increases with the frequency of cocaine use (1). Many cocaine users, especially females, engage in prostitution to support their drug use (4). Thus, cocaine use and dependence present serious problems related to the spread of AIDS (5).

The number of individuals seeking treatment for cocaine dependence increased dramatically during the 1980s (6). However, no consensus exists about how to treat these individuals (7). Patients often enter treat-

ment immediately following a binge, only to leave treatment and resume cocaine use within several days. Treatment attrition rates range from 30% to 80% for psychotherapeutic and pharmacological interventions (8, 9). Finding an intervention that will alter such cyclic cocaine use is a formidable clinical challenge.

To our knowledge, no controlled clinical trials assessing the efficacy of psychotherapy for cocaine dependence have been reported. Neurochemical data suggest that pharmacotherapies may be useful in achieving initial cocaine abstinence, and several different pharmacotherapies have been investigated with mixed results (10). The most rigorous controlled trial conducted to date was that of Gawin et al. (9). In a double-blind, random-assignment trial these authors found that 59% of patients treated for 6 weeks with desipramine hydrochloride achieved 3-4 weeks of continuous cocaine abstinence, compared with only 25% of those treated with lithium and 17% of those treated with placebo.

These findings represent an important step toward developing effective treatments, but alternatives are needed. For example, in the trial conducted by Gawin et al. (9), 41% of the patients treated with desipramine were unable to achieve 3-4 weeks of continuous cocaine abstinence, and 29% of those offered pharmacotherapy in that trial refused it.

As an alternative, our clinic has been investigating an outpatient behavioral treatment. Within a behavioral

Presented in part at the 1990 annual meetings of the Committee on Problems of Drug Dependence and the American Psychological Association. Received Nov. 21, 1990; revision received March 5, 1991; accepted March 27, 1991. From the Human Behavioral Pharmacology Laboratory, Department of Psychiatry, University of Vermont. Address reprint requests to Dr. Higgins, University of Vermont, 38 Fletcher Place—Ira Allen School, Burlington, VT 05401.

Supported by U.S. Public Health Service Treatment Research Demonstration grant DA-06113 and First Independent Research and Transition Award DA-04545 to Dr. Higgins, Research Scientist Development Award DA-00109 to Dr. Hughes, and research grant DA-06526 to Dr. Bickel from the National Institute on Drug Abuse.

The authors thank Bob Myers and Maxine Stitzer for consultation on the community reinforcement approach and contingency management interventions.

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approach, drug taking is considered a special case of operant behavior maintained by the reinforcing effects of the drug (11–13). The scientific basis for this theory comes from the vast drug self-administration literature, which demonstrates that drug taking is orderly and that the variables controlling it have generality across different types of operant behavior, species, and pharmacological types of drug dependence (14–16).

Within this conceptual framework, a strategy for treating drug dependence is to rearrange the drug user's environment so that 1) drug use and abstinence are readily detected, 2) drug abstinence is positively reinforced, 3) drug use results in a loss of reinforcement, and 4) the density of reinforcement derived from non-drug sources is increased to compete with the reinforcing effects of drugs.

Using these strategies, behavioral treatments have been effective in treating alcohol (17), tobacco (18), opioid (19), and CNS stimulant (20, 21) abuse and dependence. Behavioral interventions may also be efficacious with cocaine dependence (8, 22–25). For instance, Anker and Crowley (8) offered 67 cocaine abusers contingency contracting as an adjunct to a standard psychotherapeutic intervention. The contract stipulated that the patient would participate in urinalysis monitoring and that, in the event of a cocaine-positive specimen, a prearranged aversive consequence would follow (e.g., loss of professional license). Thirty-two patients entered the contract, typically for 3–6 months, and 31 remained abstinent for 3–6 months. In the comparison group—the 35 patients who did not enter the contract—29 terminated treatment within 4–5 sessions and none was abstinent for more than 4 weeks.

There are limitations (7) to the study by Anker and Crowley (8). First, patients were self-selected in that they chose whether to enter the contract or the comparison group. Thus, it is possible that those who entered the contract would have done well with any treatment. Second, the contract appeared to be unacceptable to the majority of patients. Third, the use of strong aversive contingencies raises ethical concerns.

The behavioral treatment in this study included two components designed to positively reinforce cocaine abstinence and to increase positive social behavior. Positive reinforcement of cocaine abstinence was achieved through a contingency management program in which incentives were provided contingent on the documentation of abstinence by urinalysis. Increasing positive social behavior was achieved through adoption of the community reinforcement approach developed for the treatment of alcohol dependence (17). The goal of that intervention was to increase the efficacy of nondrug sources of reinforcement by improving the patient's job status, family and social relations, and recreational activities (26). The overall goal of this two-pronged intervention was to use the incentives to achieve initial cocaine abstinence and retain patients in treatment, thereby gaining time to counsel patients on longer-term life style changes necessary to maintain cocaine abstinence.

This report describes results obtained in a preliminary study examining the efficacy of this behavioral treatment with 13 cocaine-dependent individuals who consecutively entered an outpatient clinic for cocaine dependence. Their results are compared with those from the next 15 cocaine-dependent individuals who consecutively entered the same clinic but were offered a 12-step drug counseling program.

METHOD

Subjects were recruited from advertisements in local newspapers, public-service announcements on television and radio, notices mailed to local professionals, and posters located throughout the local community. Subjects had to be 18 years old or older and had to meet *DSM-III-R* diagnostic criteria for active cocaine dependence for inclusion in the study. Psychosis, dementia, or a medical condition precluding employment were exclusion criteria. Use, abuse, or dependence on psychoactive substances other than cocaine were *not* exclusion criteria.

Informed consent was obtained during the intake interviews, which were approximately 3–4 hours long. The interviews included administration of the psychoactive substance abuse disorder sections of the *DSM-III-R* Criteria Checklist (27), the Addiction Severity Index (28), the Michigan Alcohol Screening Test (29), and the Addiction/Dependency Self Test (30). Questionnaires on demographics, drug history, and medical history were also completed during the interviews.

Behavioral Treatment

Patients and therapists in the contingency management program jointly selected material reinforcers for initial abstinence. Urine specimens were collected under staff observation four times a week on Mondays, Wednesdays, Fridays, and Saturdays. Specimens were screened immediately by using the Enzyme Multiplied Immunoassay Technique (Syva Corp.). All specimens were screened for benzoylecgonine, and one randomly selected specimen per week was also screened for the presence of other drugs of abuse. Breath alcohol levels were assessed at the time urine specimens were collected. Contingencies pertained only to cocaine use.

Patients were informed of their urinalysis results immediately after submitting their specimens. Specimens negative for benzoylecgonine earned points that were recorded on vouchers and given to patients. Points were worth the equivalent of \$0.15 each, although money was never provided directly to patients; instead, points were used to purchase retail items in the community. A staff member made all purchases. The first negative specimen was worth 10 points at \$0.15 per point or \$1.50. The value of vouchers for each subsequent consecutive negative specimen increased by 5 points; e.g., the second negative specimen was worth 15 points, the third was worth 20 points, the

fourth was worth 25 points, etc. To further increase the likelihood of continuous cocaine abstinence, the equivalent of a \$10.00 bonus was earned for each four consecutive negative specimens. An individual who remained continuously abstinent throughout 12 weeks of treatment could earn items worth a total of \$1,038.00, or \$12.35 per day of treatment. Specimens that were cocaine positive or failure to submit a scheduled specimen reset the value of vouchers back to the initial \$1.50, from which point they could escalate again in value according to the same schedule. Points could not be lost once earned. Items obtained were quite diverse and included ski-lift passes, fishing licenses, camera equipment, bicycle equipment, and continuing education materials. Counselors retained veto power over all voucher purchases. Purchases were approved only if the counselor felt that they were in concert with individual treatment goals.

The community reinforcement approach procedures were implemented in twice-weekly 1-hour counseling sessions for 12 weeks. Sessions focused on four general issues. First, patients with a nonabuser spouse, friend, or relative willing to participate in treatment received weekly reciprocal relationship counseling, which is a validated procedure for instructing people how to negotiate for positive changes in their relationship (31). To integrate the community reinforcement approach and contingency management procedures, the patient's significant other was telephoned immediately following each urinalysis test and informed of results. If the specimen was negative for cocaine, the spouse, friend, or relative engaged in positive activities with the patients that had been agreed upon beforehand. If the result was positive for cocaine use, he or she refrained from the agreed upon positive activities but offered the patient assistance in dealing with difficulties in achieving abstinence. Eight of the 13 patients participated in treatment with a spouse, friend, or relative. The wives of two patients, the girl friends of three, the parents of one, the aunt of one, and the stepmother of one patient participated.

Second, patients were instructed how to recognize antecedents and consequences of their cocaine use. They were counseled to restructure their daily activities to minimize contact with known antecedents, find alternatives for the positive consequences derived from cocaine use, and make explicit the negative consequences of cocaine use. Skills training, such as drug-refusal skills, was provided to those with specific deficits.

Third, unemployed patients were offered employment counseling (32). Counseling and assistance were also provided for those interested in pursuing educational goals or job changes and those with miscellaneous practical needs such as financial counseling, alternative housing, and legal and social services.

Fourth, patients were counseled to develop new recreational activities or to become involved again in those they pursued before beginning cocaine use. Counselors and patients worked together to identify these activities. This also provided an avenue for integration of the contingency management and commu-

nity reinforcement approach components. Vouchers were used to support the costs of initiating these activities.

The behavioral therapists were a male doctoral-level psychologist with 4 years of experience counseling substance abusers and a female master's-level counselor with no previous experience counseling substance abusers.

One individual in the behavioral treatment group who met *DSM-III-R* criteria for alcohol dependence received 250 mg/day of disulfiram throughout participation in this study.

12-Step Drug Counseling

Urine specimens were collected and analyzed for the patients in the 12-step program according to the same schedule used for the patients in the behavioral treatment program. Urinalysis results were not shared with patients or therapists in the 12-step program to approximate routine community outpatient drug and alcohol counseling, which often does not include regular urinalysis monitoring. When their informed consent was obtained, the patients in the 12-step program were told that urinalysis testing was for research purposes only and that the results would not be shared with their therapists. These patients received \$5.00 for each positive or negative specimen they provided.

Counseling sessions were either 2-hour group therapy sessions twice a week (the first five patients) or one group and one 1-hour individual therapy session each week (the next seven patients). The change in format from exclusively group to combined group and individual therapy was made to more closely approximate treatment offered in community drug-abuse treatment clinics as well as to prepare for the randomized trial in which the latter format would be used.

Both formats followed a 12-step model of drug counseling (33). Patients were counseled that cocaine addiction was a treatable but incurable disease. They were asked to attend at least one self-help meeting every week in addition to their regularly scheduled sessions. The regularly scheduled sessions consisted of both supportive and confrontative therapy, didactic lectures, and videos on cocaine dependence, AIDS, the disease model of addiction, and the self-help orientation. During the ninth week of treatment patients were asked to bring a family member to treatment to address family issues emanating from addiction. In the latter weeks of treatment, an aftercare plan was developed and counseling was provided on relapse prevention based on the 12-step model. Finally, patients were expected to identify a sponsor from a local self-help group by the final week of treatment.

The therapists were one male and one female counselor with master's degrees in social work and counseling and 2 and 7 years of experience in substance abuse counseling, respectively.

To our knowledge, no patient in this treatment received adjunct medications for substance abuse during their participation in this study.

Data Analysis

Comparisons between the treatment groups were made by using two-sample *t* tests for continuous variables such as use of cocaine (g/week) and Fisher's exact test and tests of proportions for dichotomous variables such as the route of cocaine administration. Continuous cocaine abstinence was analyzed by using survival analysis (34). When hypotheses predicted that the behavioral treatment would be superior (treatment retention, cocaine abstinence, and acceptability of treatment), one-tailed tests were used, and when no hypothesis was made (e.g., patient characteristics), two-tailed tests were used. Effects were considered significant at $p \leq 0.05$.

RESULTS

All 13 patients (five women and eight men) offered the behavioral treatment accepted. Twelve (three women and nine men) of the 15 patients offered drug counseling accepted. The difference in the number of patients in each group who accepted treatment was not statistically significant. Characteristics of those who accepted each type of treatment are described in table 1. The two groups differed significantly on only two characteristics: the group given behavioral therapy reported ingesting more cocaine per week before entering treatment and had more intravenous users than the group given 12-step counseling (table 1).

Treatment Retention

Eleven of the 13 patients completed 12 weeks of behavioral treatment, but only five of 12 patients completed 12 weeks of the 12-step treatment program ($p=0.03$, Fisher's exact test). In the behavioral treatment, one individual was referred to inpatient treatment due to continuous cocaine use, and a second individual terminated treatment at week 9 and returned to cocaine use.

In the group given 12-step drug counseling, one person refused group treatment; one was dropped from the program for not regularly attending therapy sessions; one refused to abstain from marijuana smoking and did not return for any subsequent sessions; one did not return for treatment after his demand for prescription medication for anxiety was denied by the staff psychiatrist and discouraged by the group; one relapsed and independently enrolled in an inpatient detoxification program; one decided he no longer needed treatment; and one was murdered.

Urinalysis Results

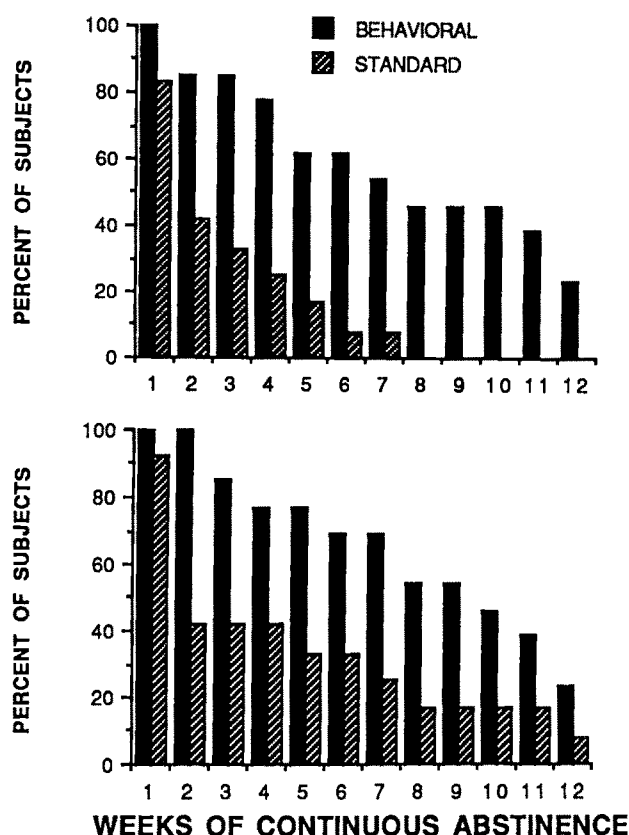
Figure 1 shows the percent of patients in each treatment who were able to achieve from 1- to 12-week periods of continuous abstinence during the 12 weeks. Patients given behavioral treatment achieved significantly

TABLE 1. Characteristics of Patients Given Behavioral Therapy or 12-Step Drug Counseling for Cocaine Dependence

Characteristic	Behavioral Treatment (N=13)	12-Step Counseling (N=12)
Age (years)		
Mean	29.0	30.5
SD	5.0	3.7
Education		
Number with 12 or more years	6	10
Number with less than 12 years	7	2
Number employed	8	8
Weekly income (dollars)		
Mean	189	309
SD	98	356
Marital status		
Number married	2	5
Number separated or divorced	4	1
Number single	7	6
Use of cocaine during most recent peak use (g/week) ^a		
Mean	10.2	3.7
SD	8.6	3.8
Primary route of cocaine use ^b		
Number who used intravenously	9	2
Number who used intranasally	3	9
Number who smoked	1	1
Duration of regular cocaine use (years)		
Mean	6.9	5.2
SD	5.0	3.9
Time since last cocaine use (days)		
Mean	8.4	7.2
SD	7.4	8.5
Michigan Alcoholism Screening Test score		
Mean	20.10	19.23
SD	14.34	14.85
Addiction Severity Index composite score		
Medical		
Mean	0.36	0.32
SD	0.38	0.29
Employment		
Mean	0.57	0.46
SD	0.30	0.30
Alcohol use		
Mean	0.21	0.27
SD	0.24	0.20
Drug use		
Mean	0.29	0.26
SD	0.06	0.09
Legal status		
Mean	0.25	0.21
SD	0.23	0.24
Family/social status		
Mean	0.31	0.44
SD	0.21	0.28
Psychiatric status		
Mean	0.46	0.46
SD	0.19	0.21
Number dependent on other drugs (DSM-III-R criteria)		
Alcohol	8	5
Marijuana	2	4
Opiates	1	0
Sedatives	1	0
Hallucinogens	1	0
Number previously treated for drug abuse	8	5

^aThe behavioral group reported ingesting more cocaine per week before entering treatment ($t=2.48$, $df=23$, $p=0.02$).

^bThe behavioral group had more intravenous users ($p=0.05$, Fisher's exact test).

FIGURE 1. Periods of Continuous Cocaine Abstinence of 13 Patients Given Behavioral Therapy and 12 Patients Given 12-Step Drug Counseling for Cocaine Dependence^a

^a Scheduled urine specimens that were not collected were treated as cocaine-positive in the upper panel and cocaine-negative in the lower panel.

longer periods of continuous abstinence than patients given 12-step drug counseling treatment, independent of whether missed specimens were treated as positive ($\chi^2=10.9$, $df=1$, $p=0.001$, upper panel) or negative ($\chi^2=7.8$, $df=1$, $p=0.005$, lower panel). For example, ten of the patients given behavioral therapy versus three of those given 12-step drug counseling achieved 4-week periods of continuous cocaine abstinence, six versus none achieved 8-week periods, and three versus none achieved 12-week periods. When missed specimens were treated as negative, the numbers for the same time periods were 10 versus five, seven versus two, and three versus one.

When all urine specimens collected were examined, 508 (92%) of the 552 from patients in the behavioral treatment program and 243 (78%) of the 312 from patients receiving counseling tested negative for benzoylecgonine ($Z=5.35$, $p<0.001$).

The two groups did not differ in other drug use analyzed as a function of treatment weeks. When collapsed across treatment weeks (table 2), the vast majority of test results were negative in both groups, but the group given behavioral therapy had a significantly lower proportion of marijuana-negative specimens

TABLE 2. Negative Test Results for Drugs Other Than Cocaine in Urine Specimens of 13 Patients Given Behavioral Therapy and 12 Patients Given 12-Step Drug Counseling for Cocaine Dependence^a

Drug	Behavioral Treatment (N=150)		12-Step Counseling (N=92)	
	N	%	N	%
Alcohol ^b	167	91	232	98
Amphetamine	144	99 ^c	91	100 ^d
Barbiturates	148	99	92	100
Benzodiazepines	135	90	86	93
Cannabinoids ^c	76	51	84	91
Methadone	150	100	92	100
Opiates	134	89	88	96

^aMissing specimens were excluded from analysis.

^bDetermined by breath alcohol levels; N=184 for patients given behavioral treatment and N=236 for those given 12-step counseling.

^cBased on N=145.

^dBased on N=91.

^eThe group given behavioral therapy had a significantly lower proportion of negative marijuana results than the group given 12-step counseling ($Z=3.71$, $p<0.001$).

than the group given 12-step drug counseling (table 2). To test whether marijuana use was related to cocaine use in the group given behavioral therapy, the relationship between the number of marijuana-positive specimens and the number of consecutive weeks of cocaine abstinence was examined. The relationship was nonsignificant, but there was a negative correlation ($r=-0.38$, $df=11$, n.s.), indicating a trend toward fewer weeks of cocaine abstinence in patients with more marijuana use.

DISCUSSION

The results obtained with the behavioral treatment in this study are promising for at least five reasons.

First, the behavioral treatment was well accepted: all of the patients who were offered this treatment accepted it. This appears to be greater than the 70% acceptance noted in the desipramine trial conducted by Gawin et al. (9) and the approximately 50% acceptance level reported by Anker and Crowley (8). Thus, this treatment may have advantages over both pharmacotherapy and other psychotherapies with regard to patient acceptability.

Second, the behavioral treatment was effective in retaining patients in treatment. Eleven of the patients in the behavioral treatment versus only five of those in drug counseling were retained through 12 weeks of treatment. The latter figure is comparable to the findings in reports from other outpatient clinics (8, 9).

Third, the behavioral treatment was effective in achieving initial cocaine abstinence. In the present study, eight of those who received behavioral therapy achieved 5 weeks or more of continuous cocaine abstinence. To our knowledge, there are no other studies on outpatient treatment of cocaine dependence that have reported docu-

mented (verified by urinalysis) periods of continuous cocaine abstinence exceeding the present results.

Fourth, few exclusion criteria were used in the present study, which may increase the potential for generalizability of results. In the trial with desipramine of Gawin et al. (9), for example, individuals with current or lifetime dependence on substances of abuse other than cocaine were excluded. Although there are good reasons for such exclusion criteria in a drug trial, they raise important concerns about generalizability of results because the majority of persons seeking treatment for cocaine dependence in our clinic and others meet criteria for other drug dependence (35).

Two differences between our clinic population and those of many clinics located elsewhere in the country, especially large metropolitan areas, merit mention because they could influence generalizability. We had no crack users, and all patients were Caucasian. How these two differences might influence the generalizability of our findings is unknown. However, it is important to keep in mind that although crack use and related problems in large metropolitan areas have appropriately garnered much attention, use of cocaine hydrochloride by Caucasians still makes up the majority of cocaine use in the United States (2).

Fifth, the majority of the patients given behavioral treatment were intravenous cocaine users. A treatment that is acceptable to intravenous drug users, retains them in treatment, and is able to maintain substantial periods of abstinence could be important in current efforts to curtail the spread of AIDS.

At least three obvious criticisms can be raised about this study. First, it was not a randomized trial. Differences between the groups given behavioral treatment and 12-step counseling may have been due to unmeasured differences in patient characteristics, time of treatment, or some other uncontrolled variable. We acknowledge the importance of a randomized trial and currently have one underway comparing these same treatments. That aside, we do not know of any differences in patient characteristics to account for the outcome differences observed. If anything, we would expect that the fact that nine of the 11 patients receiving 12-step counseling used cocaine intranasally rather than intravenously would favor a better outcome for these patients. As for differences in the time when patients entered the behavioral treatment and 12-step programs, we do not know of anything local that would have influenced treatment (e.g., cocaine arrests or major cocaine interdictions). In addition, the treatment periods of the two groups overlapped by 2.5 months, and all patients were treated in a 5-month period.

In addition to patient characteristics, there are important differences in many aspects of the two treatments (e.g., degree of family involvement) that may have contributed to the differential treatment outcomes observed. However, because this study was designed to compare two general treatment approaches rather than to assess the influence of specific treatment characteristics, the contribution of such differ-

ences to treatment outcome will have to be assessed in future studies.

A second potential criticism is that the behavioral treatment depended on contrived and costly incentives. In our opinion, the incentives were no more contrived than the cocaine with which they were designed to compete. The rationale behind the use of material incentives is to arrange conditions that encourage initial abstinence and retain individuals in treatment, thereby providing more time for the difficult task of getting them involved with more naturalistic contingencies of reinforcement for abstinence. The costs of the incentives (a maximum of \$12.35/day) pale when considered against the costs of inpatient hospitalization or of diseases such as AIDS that are associated with intravenous drug use.

Of course, an incentive program of even modest cost is likely to be impossible in many community clinics. However, the potential utility of incentive programs should not be hastily dismissed on that basis. For example, community businesses might be willing to donate retail items for use as incentives, or special access to community recreation and other facilities (e.g., swimming pools, gymnasiums) might prove to be effective incentives. With some individuals, consistent use of social reinforcement for abstinence might be sufficient; that is, material incentives may be unnecessary for some individuals. Through creative planning, community cooperation, and individualized treatment plans, it may be possible to establish effective incentive programs at minimal or no cost to clinics.

A third potential criticism is that patients given the behavioral treatment continued to use other drugs while abstaining from cocaine. Although there was significantly more marijuana use among the patients in the behavioral program than those in the 12-step program, there was relatively little use of other drugs (table 2). Moreover, the marijuana use that did occur did not appear to contribute to the significant periods of cocaine abstinence that patients in that treatment were able to achieve; that is, marijuana was not functioning as a substitute for cocaine. If that were the case, cocaine abstinence and marijuana use should have been positively related, but marijuana use and cocaine abstinence were not significantly related, and the coefficient for that relationship was negative. The absence of evidence for drug substitution in this study is consistent with results in previous studies in which contingent reinforcement was provided for abstinence from a single drug class (36, 37).

Patients in the behavioral program were counseled to abstain from other drug and alcohol use, but it was not required to remain in treatment. There were two reasons for placing contingencies on cocaine use only. First, cocaine dependence was the problem for which patients requested treatment and, despite clinical beliefs, there is no empirical evidence demonstrating that total drug abstinence is a necessary prerequisite to achieve cocaine abstinence. Second, we deemed it important in this preliminary assessment of a contingency

management intervention with cocaine use to focus carefully on the target behavior. The efficacy for achieving cocaine abstinence with contingencies requiring only cocaine abstinence versus abstinence from all drug use is an important topic for future investigation.

Finally, although the results obtained with the behavioral treatment in this pilot investigation look promising, they are preliminary and must be treated cautiously. A randomized trial comparing these same treatments is ongoing in our clinic.

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HIV Seroprevalence Among Patients Admitted to Two Psychiatric Hospitals

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***Objective:** The authors determined the seroprevalence of HIV-1 among patients admitted to two psychiatric hospitals in New York City. **Method:** Patients consecutively admitted to an acute psychiatric unit in Manhattan and a large state hospital in Queens were anonymously tested for HIV-1 antibodies from December 1989 through July 1990. Test results were linked to age, gender, ethnicity, and two risk behaviors: male homosexual activity and injection drug use. **Results:** Blood was obtained from 83.0% of the eligible patients. The prevalence of HIV was 5.5% (25 of 451). Black patients accounted for 38.0% of the patients tested and 76.0% of positive results (N=19), a rate of 11.1% for this group. The rate of seropositivity was comparable in women and men. Clinicians had charted risk behavior for nine (36.0%) of the 25 HIV-positive patients. Infection control records suggested that clinicians were aware of seven (28.0%) of the positive cases. **Conclusions:** One in every 18 patients admitted to two public psychiatric hospitals in New York City was HIV positive. Clinical staff largely failed to identify HIV-positive patients. Ethnicity and a history of homosexual activity among men or use of injected drugs were strongly associated with seropositivity. This pattern of infection may be linked to needle sharing and/or sexual activity with partners who have shared needles. Future research should clarify how psychiatric illness affects risk-taking behavior, focus on improving detection by clinicians, and identify effective prevention strategies in this population. (Am J Psychiatry 1991; 148:1225-1230)*

We have seen an alarming increase in HIV infection among the severely mentally ill. The 4,000-bed state hospital system in New York City identified its first case of AIDS in 1983. By 1988, 24 patients who were openly tested that year were positive for HIV-1 antibodies, and in 1989 the number had increased to 53 newly tested HIV-positive patients (1). In addition to known cases, an unknown number of infected psychiatric patients with risk-taking histories who do not consent to HIV antibody testing or who do not report risk behaviors are being cared for in psychiatric hospitals.

Presented at the 143rd annual meeting of the American Psychiatric Association, New York, May 12-17, 1990. Received Nov. 6, 1990; revision received Feb. 19, 1991; accepted March 18, 1991. From the New York State Psychiatric Institute and Washington Heights Community Service, New York. Address reprint requests to Dr. Cournos, New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032.

This study was funded by NIMH grant MH-46251 and the New York State Office of Mental Health.

The authors thank Diane Engel, M.S.W., Michael Georgescu, Diana Hartel, Ph.D., Nancy Hopkins, R.N., Jim Johnson, Ph.D., Ellie Schoenbaum, M.D., and Zena Stein, Ph.D.

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The severely mentally ill as a group are vulnerable to HIV infection because of comorbidity with substance abuse (2). Psychiatric diagnosis and substance abuse appear to be related (3-6), leading many investigators to hypothesize a self-medication effect (3, 5-7). Chronic substance abuse may also precipitate and exacerbate psychosis (8, 9). Smokable cocaine (crack) and injection drugs are among the substances used by psychiatric patients and are highly associated with HIV infection (10-15).

Unsafe sexual behavior, including sex with strangers or with partners who inject drugs, has also been reported among the severely mentally ill (16-23), and psychiatric symptoms are likely to affect patients' perceptions of their own HIV risk and efficacy in preventing infection (24).

At present little is known about the prevalence of HIV infection among psychiatric patients. Zamperetti et al. (25) reported that 6.5% of 475 patients admitted to a psychiatric ward in Milan over 2 years were HIV positive. In an ongoing study of patients admitted to acute care psychiatric units in a private hospital in New York City, Sacks et al. found that of 254 patients between the ages of 18 and 55 years who were anony-

mously tested for HIV-1, 20 were positive, a rate of 7.9% (VI International Conference on AIDS, 1990). One-half of the seropositive patients reported male homosexual activity, and one-quarter reported either injection drug use or sex with a partner who injected drugs. In another ongoing study, nine (7.3%) of 124 patients admitted to a psychiatric unit for the homeless were reported positive for HIV-1 (Empfield et al., VI International Conference on AIDS, 1990).

METHOD

Patients and Procedure

We tracked patients between the ages of 18 and 59 years who were consecutively admitted to two psychiatric hospitals in New York City from December 1989 through July 1990. One site was a 22-bed acute care unit at an academic medical center in northern Manhattan mandated to accept all patients referred from the local catchment area; 133 eligible patients were admitted to this unit. The other site was a large state hospital providing acute and chronic care to the borough of Queens; 413 eligible patients were admitted here. Both settings are state funded and mandated to treat severe mental illness. Most patients are either uninsured or have Medicaid. Any patient with a primary diagnosis of either dementia or substance abuse is excluded by policy from admission.

Following current federal regulations for anonymous sampling (26), we obtained discard blood samples from blood drawn for routine purposes at the time of admission. Patients whose discard blood was not obtained on admission were tracked for subsequent blood workup. Samples could not be obtained for every patient because of patient refusal of blood tests, patient discharge before blood drawing, or insufficient quantity. Blood samples were obtained for 456 of the 546 patients. We kept a record of every patient admitted so that we would obtain only a single sample of blood from each patient even if individual patients were admitted more than once during the study period. This patient roster was destroyed after all the discard blood samples were obtained.

Patient chart number, date of birth, admission diagnosis, and number of previous psychiatric hospitalizations were obtained from each patient's chart and recorded on the top half of a two-part form to obtain profiles of the eligible patients unlinked with HIV status. Age range, gender, ethnicity, known use of injected drugs, and history of homosexual activity among men were obtained from the patient chart and recorded on the lower half of the form. Because few Asian patients are admitted to either hospital, Asians were grouped with Caucasians to avoid the possibility of identifying any HIV-positive Asian patient. After demographic and risk factors were ascertained, the patient identification (upper) section of the form was removed and a six-digit bar-code number was affixed to the

lower section to link the blood sample with the demographic and risk factor data.

The blood samples were stored, frozen, and sent in batches of at least 25 to the New York Blood Center for antibody testing. Specimens that were shown to be reactive by enzyme-linked immunosorbent assay (ELISA) were tested with the Western Blot and then classified according to current recommendations of the Centers for Disease Control (27). A specimen was considered positive if antibodies to two of the following were detected: p24, gp41, and gp120/160. The presence of any single band on the Western Blot constituted an indeterminate result. Because the sampling was anonymous, obtaining a second specimen for retesting from patients whose test results were inconclusive was not possible.

Data Analysis

A group profile of the tested patients, unlinked to their blood specimens, provided descriptive clinical data, including admission diagnosis and number of previous psychiatric hospitalizations. Linking of the blood test results with the patients' demographic characteristics and HIV risk behaviors provided prevalence rates within subgroups. All data were measured at either a nominal or ordinal level; therefore, contingency table analysis was used to interpret the data. Chi-square and Bartholomew's tests were performed, and odds ratios were used to estimate relative risk. Adjusted odds ratios were derived from logistic regression coefficients. Statistical significance was expressed in exact values, with the exception of the result of the Bartholomew's test, which was expressed as significant or not significant. The criterion for significance was set at an alpha level of 0.05.

RESULTS

Of the 456 samples sent to the New York Blood Center for antibody testing, three were reported to be too small for testing. Of the 453 samples tested, 28 (6.2%) were reactive according to ELISA. Two of these showed indeterminate results on Western Blot and were omitted from the analysis of relative risk and serostatus. Of the remaining 26 samples that were reactive on ELISA, 25 were confirmed positive by Western Blot. This results in a seroprevalence rate of 5.5% (25 of 451). The distribution of positive results is shown in table 1. One sample that was reactive according to ELISA was negative according to Western Blot.

Of the 133 eligible patients admitted to the 22-bed Manhattan unit during the study period, 128 were tested for HIV. Of the 413 eligible patients admitted to the state hospital in Queens during the study period, 325 were tested. Eight (6.3%) of the 128 tested samples from the acute unit were positive, and 17 (5.2%) of the 325 tested samples from the state hospital in Queens were positive. The rates at the two sites were not statis-

TABLE 1. Association of HIV Infection With Injection Drug Use, Homosexual Activity Among Men, and Demographic Factors in 451 Psychiatric Patients

Variable	Patients Tested ^a	HIV-1 Antibody Positive		Chi-Square Analysis			Unadjusted Odds Ratio		Adjusted Odds Ratio		p
		N	%	χ^2	df	p	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	
Age (years) ^b				0.46 ^c	3	n.s.	1.35	0.55–3.32	1.27	0.48–3.34	0.62
18–29	142	9	6.34								
30–39	155	9	5.81								
40–49	110	5	4.55								
50–59	44	2	4.55								
Ethnicity ^d				17.79	2	0.0001	5.63	2.20–14.40	6.33	2.39–16.73	0.0002
Black	172	19	11.05								
Hispanic	115	5	4.35								
Caucasian/Asian	163	1	0.61								
Sex				0.22	1	0.64	1.21	0.54–2.72	2.23	0.84–5.93	0.11
Male	237	12	5.06								
Female	214	13	6.07								
Injection drug use				5.97 ^e	1	0.02	3.76	1.41–10.06	—	—	—
Identified	39	6	15.38								
Not identified	412	19	4.61								
Homosexual activity in men (N=237)				3.16 ^e	1	0.08	4.67	1.14–19.07	—	—	—
Identified	18	3	16.67								
Not identified	219	9	4.11								
Any risk factor				12.18 ^e	1	0.0005	4.76	1.99–11.40	7.58	2.69–21.36	0.0001
Identified	54	9	16.67								
Not identified	397	16	4.03								
Total	451	25	5.54								

^aTwo patients had indeterminate results and were omitted from this analysis.^bComparison groups for calculating the odds ratios for age were 18–39 and 40–49 years.^cBartholomew's test for increasing proportions (trend).^dN=450 because ethnicity was not recorded for one seronegative patient. Comparison groups for calculating the odds ratios for ethnicity were black and nonblack.^eWith continuity correction.

tically different ($\chi^2=0.18$, $df=1$, $p=0.67$). Site as a variable was omitted from further analysis because of this nonsignificant difference.

In total, we tested 453 of the 546 admitted patients, or 83.0%. There were no significant differences in age or gender between the patients whose blood we obtained and those we did not. Caucasian and Asian patients were represented somewhat less among the blood samples collected than among those not collected. Blood was not obtained for 15.5% of the black patients and 10.0% of the Hispanics, whereas for the Caucasian/Asian group, blood samples for 21.6% were not obtained ($\chi^2=8.12$, $df=2$, $p=0.02$).

As a group, the 456 sampled patients had the following admission diagnoses: schizophrenia, N=206 (45.2%); schizoaffective disorder, N=39 (8.6%); affective disorder, N=114 (25.0%); other psychotic disorders, N=53 (11.6%); all other diagnoses, N=42 (9.2%), including two patients with unknown diagnoses. Number of known previous psychiatric hospitalizations was as follows: zero hospitalizations, N=65 (14.3%); one hospitalization, N=49 (10.7%); two to five hospitalizations, N=297 (65.1%); more than five hospitalizations, N=45 (9.9%). There were no significant differences be-

tween the sampled patients and the patients whose blood was not obtained in diagnosis ($\chi^2=0.72$, $df=3$, $p=0.87$) or number of previous hospitalizations ($t=0.44$, $df=109.8$, $p=0.66$).

When we examined the linked risk histories of the seropositive patients, clinicians had identified risk behavior in nine (36.0%) of the 25 patients. Among the 12 HIV-positive men, six (50.0%) had known risk behaviors. Three (25.0%) used injected drugs, and three (25.0%) had histories of homosexual activity. Among the 13 HIV-positive women, three (23.1%) injected drugs. Of the 428 seronegative patients, 33 (7.7%) were identified as injection drug users. Of the 225 seronegative men, 15 (6.7%) had histories of homosexual activity. Relative risk estimations were derived with unadjusted odds ratios to compare the risks of testing positive for HIV-1 antibodies among the patients with and without identified risk factors. Unadjusted odds ratios calculate relative risk for each factor without controlling for effects of other risk variables. The unadjusted odds ratios showed that identified injection drug users were almost four times as likely to be seropositive as patients without histories of injection drug use. Overall, the risk of being seropositive was five times as

high for the patients with known histories of at least one of the measured risk behaviors as for those who did not have such histories. The association of serostatus with demographic and behavioral risk factors is presented in table 1.

Using multiple logistic regression to simultaneously analyze the effects of several independent variables on HIV status, we found ethnic group and behavioral risk factors to independently contribute to the likelihood of being HIV seropositive. The adjusted odds ratios show that the risk for blacks was six times that of subjects in other ethnic groups, and the chance of having a positive Western Blot result for patients with one or more behavioral risks was seven and one-half times the risk for other patients.

The unadjusted and adjusted estimations of relative risk demonstrate essentially the same relationship between risk factors and HIV seropositivity. Thus, ethnicity and behavioral risk factors independently increase the likelihood of testing positive for HIV-1 antibodies.

DISCUSSION

Most of the patients in our study were psychotic and had multiple psychiatric admissions. The most common clinical diagnosis was schizophrenia, and 75.0% of the patients had had two or more hospitalizations before the index admission. The 5.5% prevalence of HIV indicates that certain severely mentally ill patients are at risk for HIV infection. A history of risk behavior was charted by clinicians for only 36.0% of the seropositive patients. Despite this low rate of recorded risk, a history of risk behavior, either homosexual activity among men or injection drug use, predicted HIV seropositivity.

The results of this study suggest several conclusions regarding the pattern of HIV infection among an urban, severely and chronically ill psychiatric population. First, the highest rates of infection are among black patients. In our group, one in nine black patients was HIV positive. Second, women are as likely to be infected as men. Third, a record of risk behavior is likely to be found for only a minority of patients.

Having learned that women in this population are as likely to be infected as men, we must make active efforts to identify their risk-taking behaviors, which include having sexual partners who inject drugs. Recent data (28) show that for New Jersey and New York, HIV/AIDS is the leading cause of death for black women aged 15–44 years. This HIV/AIDS death rate is nine times that for Caucasian women of the same age. It is not clear to what extent differences in infection rates between black, Hispanic, and white women are caused by differences in risk behavior, exposure to infected sexual or needle-sharing partners, and biological vulnerability to HIV infection.

The pattern of infection we found also suggests a link to injection drug use. The New York City Department of Health (29) reported that for 49.7% of the black and Hispanic men in New York City with known cases of

AIDS, use of injected drugs is the primary risk factor. Among all women with AIDS in New York City, injection of drugs is the primary risk factor for 61.5% and sex with men at risk is the primary risk factor for 24.1%. In contrast, among white men with AIDS, only 12.4% report injection of drugs as their primary risk behavior. Given that in our group 76.0% of the seropositive subjects were black and 52.0% were women, injection of drugs and having sexual partners who inject drugs are likely to be major factors in how psychiatric patients acquire HIV infection.

The rate of HIV infection in our subjects does not simply mirror other rates in the New York City area. The rate of 5.5% in our subjects is intermediate among reported rates in a number of clinical settings in New York City. For example, the New York City Department of Health (30) performed prevalence studies in 1988–1989 and found the following lower rates of HIV infection among 6,325 tested patients: abortion clinics, 1.6%; sentinel hospital A, 1.4%; sentinel hospital B, 2.7%. A 1988 study of the mentally retarded living in the metropolitan New York City region (31) showed no HIV-positive subjects among 241 clients whose blood was tested. On the other hand, our rate was lower than that reported for the high-risk patients seen in New York City clinics for sexually transmitted diseases (32). There, 8.8% of 8,931 patients tested in 1988 and 1989 were positive for HIV-1 infection.

Our study sites are in areas of New York City with low to moderate rates of AIDS cases. In June 1990, the rates of AIDS cases in the city varied by zip code from 57 cases to 1,802 cases per 100,000 population (29). The range in the neighborhoods we drew our patients from was 65 to 348 cases per 100,000 population. Significantly higher rates might be found on psychiatric units with patients from areas of the city with higher rates of AIDS. The reported seroprevalence rate is, nevertheless, an estimate of the minimum percent of AIDS cases we will eventually see in our population.

Anonymous seroprevalence studies have advantages and disadvantages. An anonymous study does not identify the patient or require that any extra blood be drawn. Because there is no impact on the patient, consent is not required. This method allows investigators to test larger groups of patients, thereby increasing statistical power and representativeness without self-selection bias and without interfering with clinical judgment about the risks and benefits of testing for any individual patient. Patients who might otherwise refuse HIV testing or be unable to give informed consent can be included. On the other hand, because the study is not performed with the consent of the patient, it is impossible to conduct structured diagnostic or risk assessment interviews. Our study therefore had to depend on the information available in hospital records. We did not link blood samples to psychiatric diagnosis because admission diagnoses are not as reliable as those established by research interviews. We did not want to draw erroneous conclusions about the relationship between HIV status and psychiatric diagnosis.

The anonymous survey method poses an ethical problem because it determines the presence of HIV-positive people within a group without allowing identification, counseling, and medical care. Identification of HIV-positive psychiatric patients might result in additional stigmatization of this chronically and severely ill population. These disadvantages had to be weighed against the value of establishing their prevalence of HIV. We concluded that the information gained would be essential to planning for the needs of a large number of severely mentally ill patients and therefore the benefits of obtaining a full epidemiological picture outweighed the disadvantages of the method.

Sampling limitations also may have affected our results. Because Caucasians and Asians were overrepresented among the 17.0% of admitted patients for whom we did not obtain blood, we may have overestimated HIV prevalence in our subjects. On the other hand, our findings probably underestimate the prevalence of HIV-1 among psychiatric patients from neighborhoods in New York City with higher concentrations of HIV. We did not extract chart information about sexual partners who injected drugs or were HIV positive. The existing literature led us to bias our questionnaire in favor of recording risk behavior among men. In addition, chart review may have underestimated the clinicians' knowledge of their patients. Clinical staff may have had knowledge about risk behavior that they did not record, either to maintain confidentiality or because it seemed irrelevant for charting purposes.

Independent of our study, the clinicians at the two hospitals involved in our investigation are required to report known HIV-positive patients to hospital infection control nurses. During the same period in which our anonymous study determined 25 patients to be HIV positive, the infection control nurses recorded seven HIV-positive patients. We cannot validate the accuracy of the infection control records, and we do not know whether any of the seven reported cases were among our patients for whom blood samples were not available. However, this observation suggests that, at best, clinicians were aware of only seven of the 25 HIV-positive patients identified by the anonymous survey.

Clinical staff at the large state hospital reported two HIV-positive patients to infection control committees. This compares to the 17 seropositive patients who were found by the anonymous study. On the small acute care unit, five HIV-positive patients were reported by clinical staff to the infection control committee, and the anonymous study found eight seropositive patients. Therefore, the low rates of risk behavior charted by clinicians seem consistent with the small number of HIV-positive patients identified by them.

Risk behaviors were detected for all the HIV-positive patients reported to the infection control committees. Of the seven patients who were known to be HIV positive, two (28.6%) were men and five (71.4%) were women. One man was identified as having injected drugs, and one had a female sexual partner with HIV/AIDS. One of these patients was black, and one was

Hispanic. Of the five women identified by clinicians as HIV positive, two were black and three were Hispanic. Among the women, three were identified as users of injected drugs, three used cocaine, one had a history of prostitution, and four were identified as having sexual partners who injected drugs. It is clear that once someone tests positive for HIV, risk-taking behaviors are more aggressively investigated. However, many infected people are passing through undetected, making early intervention impossible.

When risk taking is identified, appropriate counseling and serologic testing with patient consent is indicated. This should be done in the context of clinical care. We believe the issue of mandatory testing is not one that the mental health system should attempt to address independently. Psychiatric patients deserve the same consideration as other groups when individual rights and public health interests are balanced. For most groups, the current approach is to encourage testing with informed consent but not to require it. Given sufficient clinical attention, many infected patients can be identified. The small acute care unit in our study, which has a high physician-to-patient ratio, was more successful at this task than the large state hospital, which has less physician oversight. However, even at the state hospital, it may be possible to overcome this problem by developing systematic procedures for inquiring about HIV-risk behavior.

In an ongoing study, we are collecting seroprevalence data from homeless and long-stay units and risk assessment interview data from multiple units at the two hospitals. These data will allow us to develop a prediction model for HIV infection and AIDS cases and to examine how psychiatric symptoms and risk are related. We hope to find ways to protect the considerable number of risk-taking psychiatric patients who are antibody negative and to reduce the risk of transmission by those who are already infected. We believe these efforts are uniquely within the province of psychiatry and urge additional efforts in this area.

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Comparative Phenomenology of Early-Onset Versus Late-Onset Panic Attacks: A Pilot Survey

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Studies of panic attacks in older adults are virtually nonexistent. The authors surveyed 520 adults with panic attacks; 445 were younger than age 55, 57 were 55 years old or older but had their first panic attack before age 55, and 18 were 55 years old or older and had their first panic attack at age 55 or later. The respondents with late-onset panic attacks reported fewer symptoms during their attacks and were less avoidant than both groups of respondents with early-onset panic attacks.

(Am J Psychiatry 1991; 148:1231-1233)

Increasing research efforts have been directed in recent years toward better understanding of the epidemiology and phenomenology of panic disorder (1-3). A comprehensive survey of the literature (4), however, indicated that such research has been lacking in older adults. In view of the evidence that many patients with this syndrome are inadequately treated (5, 6), a lack of such studies in the elderly might indicate that panic disorder may be self-limiting with advancing years. Alternatively, we might be failing to observe this syndrome in older people. Further, with the exception of a recent case report (7), there is no evidence in the literature that panic disorder can begin in old age.

The purpose of the present survey was to look at the phenomenology of panic attacks in older patients compared with younger patients and to inquire whether a syndrome of recurrent panic attacks can begin in old age.

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Supported by NIMH grant MH-40118, the Veterans Administration Medical Research Service, and a grant from the Upjohn Company.

METHOD

Volunteers were solicited through radio and newspaper advertisements to participate in treatment studies of panic disorder and agoraphobia in our anxiety disorders program. A self-report panic/agoraphobia questionnaire survey was mailed to subjects who volunteered to participate in such studies.

The first part of the questionnaire concerned biographical information, including age and sex. The second part of the questionnaire, the Stanford Agoraphobia Severity Scale (8), asked the subjects to rate how they would most typically behave in ten different situations on a scale of 0-4 on which 0=Can do without anxiety, 1= Can do with mild anxiety, 2=Can do with severe anxiety, 3=Can do only with extreme terror, and 4=Cannot do under any circumstances. The 10 situations were 1) shopping alone in a large department store, 2) being alone at home for 2 days, 3) driving a car alone 10 miles on a freeway like California highway 101, 4) walking alone for 1 mile away from home, 5) shopping alone in a large grocery store, 6) being alone in a crowded place like a movie theater or church, 7) crossing a busy street alone, 8) eating a complete meal alone at a casual family restaurant, 9) using public transportation alone, and 10) waiting in a long line at a bank or the department of motor vehicles. The avoidance items significantly correlated with each other, with all *r* values exceeding 0.30. A factor analysis identified only one factor with an Ei-

TABLE 1. Characteristics of Respondents With Early- or Late-Onset Panic Attacks

Characteristic	Onset Before Age 55				Onset After Age 54 (N=18)	
	Respondents Younger Than 55 (N=445)		Respondents 55 Years Old or Older (N=57)		Mean	SD
	Mean	SD	Mean	SD		
Age (years)	36	8.5	62	4.4	66	6.6
Age at first panic attack (years)	25.5	10.3	30.4	13.6	61.7	6.3
Number of symptoms in a bad panic attack ^a	9.2	3.1	8.5	3.5	6.8	3.4
Total avoidance behavior score ^b	13.7	9.8	14.3	10.4	6.3	7.1

^aRespondents with late-onset panic attacks had significantly fewer symptoms than both groups of respondents with early-onset panic attacks ($F=5.6$, $df=2$, 516, $p<0.005$; post hoc Duncan).

^bA higher score indicates more avoidance behavior. Respondents with late-onset panic attacks had a significantly lower mean score than both groups of respondents with early-onset panic attacks ($F=3.5$, $df=2$, 441, $p<0.05$; post hoc Duncan).

genvalue greater than 1, suggesting that the items measured one domain. An intraclass correlation coefficient was used to determine the test-retest reliability for the summed score of all 10 avoidance items for 45 subjects who were given the same questionnaire within 45 days and was found to be 0.92. The third part of the questionnaire asked about a history of panic attacks, age at onset of such attacks, number of symptoms in a bad attack, and frequency of such attacks. Finally, subjects were asked to document whether some of their panic attacks occurred "out of the blue" (spontaneous panic attacks).

RESULTS

Of the 1,746 subjects who were mailed the questionnaire, 1,051 (60%) responded. Only the subjects who reported that some of their panic attacks occurred "out of the blue" and who provided the age at onset of their first panic attack were included in the data analysis. This reduced the number of respondents to 520. Of these, 445 subjects were less than 55 years of age and the remaining 75 were 55 years old or older. The latter group was further subdivided into those reporting the age at onset of their first panic attack before 55 ($N=57$) and those reporting it at age 55 and older ($N=18$).

Of the 445 respondents younger than 55, 331 (74%) were women; 43 (75%) of those older than 55 who had their first panic attack before age 55 and 12 (67%) of those who had their first attack at age 55 or later were women. As can be seen in table 1, the two groups of respondents who had their first panic attacks before age 55 reported significantly more panic symptoms during a bad panic attack as well as more avoidance behavior than those who had their first panic attack at age 55 or later. There was no statistical difference in weekly frequency of panic attacks across these three groups ($F=0.67$, $df=2$, 496, n.s.). Correlating total avoidance behavior with duration of illness yielded a nonsignificant correlation of $r=0.02$, $df=444$, $p=0.6$.

DISCUSSION

Our findings that older respondents with late-onset panic attacks had fewer panic symptoms as well as less avoidance behavior seem to be expected in view of earlier findings of a decline in central noradrenergic function with advancing age, including a significant drop in locus ceruleus neuronal activity (9), as well as theoretical formulations that such a decline in symptoms should be expected in older people (10). However, an expectation of such a decrease in symptoms with advancing age is not borne out in our group of older respondents whose first panic attack occurred before they were 55. The symptoms of these respondents seemed to resemble those of the respondents who were younger than 55. Given a nonsignificant correlation between the duration of illness and avoidance behavior in the total study group, the conditioned responses acquired at a younger age in the respondents who were 55 or older may be responsible for perpetuating similar symptoms in spite of a decline in central noradrenergic function.

Because our survey did not ask respondents about the presence of depression, it is not possible to evaluate its causative or contributory role in late-onset panic attacks. However, our survey results, although preliminary, raise several interesting questions. For example, given the present thinking that a syndrome of recurrent panic attacks probably suggests a genetically determined vulnerability usually manifested in the early 20s, did the respondents who were 55 years old or older when they had their first panic attack have that vulnerability? If so, why did they develop panic attacks at such a late stage in their life? Alternatively, is it possible that late-onset panic attacks are a distinct variant and occur primarily because of environmental influences or traumatic life experiences? Only more detailed investigations of this syndrome in a prospectively studied sample can answer such questions.

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Serum Nortriptyline Levels in Nursing Mothers and Their Infants

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The nortriptyline levels of seven depressed mothers and their breast-fed infants were obtained. Nortriptyline was not detected in the infants' sera. However, two of four infants evaluated developed low concentrations of 10-hydroxynortriptyline. No adverse effects were observed. (Am J Psychiatry 1991; 148:1234-1236)

The incidence of depression in postpartum women is 10% to 15% (1). The only data to guide physicians in antidepressant treatment of nursing mothers consists of isolated case reports. Few drugs have been evaluated, and only a small number of studies have assessed the serum levels developed by nursing infants.

In this paper we present serum concentrations obtained from a series of seven nortriptyline-treated nursing mothers and their infants. We selected nortriptyline because of its low relative anticholinergic potency and well-documented therapeutic serum levels (50–150 ng/ml).

Reports of nursing mothers treated with amitriptyline (2–4) showed that their infants had nondetectable blood levels of amitriptyline/nortriptyline and no adverse effects. Bader and Newman (2) obtained maternal and infant serum and breast milk after 8 weeks of treatment with amitriptyline (100 mg/day). The mother's total tricyclic levels were 142 and 187 ng/ml in serum and milk, respectively. Neither amitriptyline nor nortriptyline was detectable in the infant's serum with a measure sensitive to 10 ng/ml. Brixen-Rasmussen et al. (3) treated a mother with amitriptyline (75 mg/day) at 3.5 months postpartum. Total serum tricyclic levels were low in two maternal samples (121 and 111 ng/ml) and were nondetectable in the infant. Erickson et al. (4) studied a mother who had taken 150 mg/day of amitriptyline for 3 weeks; her total tricyclic level was 236 ng/ml. The total serum tricyclic level of the infant was less than 28 ng/ml (not detectable).

Nursing concentrations of the major metabolite of nortriptyline, 10-hydroxynortriptyline, have not been previously studied to our knowledge. This metabolite occurs as geometrical *E* and *Z* isomers. In adults, the serum concentrations of *E*- and *Z*-10-hydroxynortriptyline are 150%–300% and 5%–22% of nortriptyline, respectively (5). These metabolites are significantly less active than nortriptyline. *E*- and *Z*-10-hydroxynortriptyline have half as much potency as inhibitors of the neuronal uptake of norepinephrine (6) and about 5% of the anticholinergic efficacy (7).

To our knowledge, this study is the first attempt to 1) evaluate nortriptyline levels in a series of mother-baby pairs, 2) use a sensitive nortriptyline assay (limit of detectability=4–5 ng/ml), and 3) assess mother-baby 10-hydroxynortriptyline levels.

METHOD

The mothers met the *DSM-III* criteria for major depression, and none took any other prescribed drugs. Informed consent for treatment with nortriptyline and blood sampling was obtained. The healthy infants were 6 months of age or less at the time of serum sampling. All were full-term except infant 5, the healthy 7-lb, 9-oz product of a 36-week gestation. The infants were fully breast-fed except infants 1 and 4, who received formula during one feeding per day.

The nighttime nortriptyline dose was increased until the mothers experienced marked reduction in depressed mood and vegetative symptoms. We collected a steady-state blood sample from each mother after a minimum of 15 days at a stable dose. Cooper and Simpson (8) found that most of their subjects had reached steady state by day 7 of nortriptyline administration; for every individual, nortriptyline levels on days 13–15 were within 10% of the average value. The infants were nursed within 3 hours before sampling. The nursing serum concentrations are summary values that resulted from feedings throughout the day.

Samples 1–3 were analyzed by the National Psy-

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Supported in part by NIMH First Independent Research Support and Transition Award MH-44287 to Dr. Wisner, and by NIMH grant MH-30915 to Dr. Perel.

This paper is dedicated to the memory of Joaquim Puig-Antich, M.D. The authors thank Maureen Granberry for drawing the infant blood samples.

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TABLE 1. Serum Concentrations of Nortriptyline and E- and Z-10-Hydroxynortriptyline in Nursing Mothers and Their Infants

Pair	Infant's Age (weeks)		Mother's Nortriptyline Regimen			Serum Levels (ng/ml) ^a		
	Mother's Medication Begun	Serum Sampling	Dose (mg/day)	Time at Dose (days)	Time Since Last Dose (hours)	Nortriptyline	E-10-Hydroxynortriptyline	Z-10-Hydroxynortriptyline
Pair 1								
Mother			80	16	12	77	—	—
Infant	8	11				<5	—	—
Pair 2								
Mother			75	16	15	110	—	—
Infant	11	14				<5	—	—
Pair 3								
Mother			50	120	15	49	—	—
Infant	9	26				<5	—	—
Pair 4								
Mother			75	60	14	47	47	12
Infant	8	21				<4	<4	<4
Pair 5								
Mother			70	20	13	160	105	22
Infant	Newborn	3				<4	7	5
Pair 6								
Time 1								
Mother			75	15	13	126	144	25
Infant	Newborn	8				<4	<4	11
Time 2								
Mother			75	85	12	146	75	7
Infant	Newborn	18				<4	<4	<4
Pair 7								
Mother			50	50	17	164	37	22
Infant	14	20				<4	<4	<4

^aValue of <4 or <5 denotes concentration below the limit of detectability.

chopharmacology Laboratory (Knoxville, Tenn.) by means of the gas chromatographic nitrogen-specific detector method. The interday coefficient of variation for nortriptyline for high and low control samples was 5.5% and 6.2%, respectively. Samples 4–7 were analyzed in the laboratory of one of us (J.M.P.) by a high-performance liquid chromatographic method with ultraviolet detection at 215 nm. The limit of detectability was 4–5 ng/ml (9). The interday coefficient of variation for nortriptyline for high and low control samples was 2.2% and 4.1%, respectively. A prior assessment of interlaboratory reliability yielded an intraclass correlation coefficient of 0.91.

RESULTS

Table 1 summarizes the results. No nortriptyline was detected in the infant sera, and the maternal concentrations ranged from 47 to 164 ng/ml. 10-Hydroxynortriptyline was detected at low levels in infants 5 and 6, the youngest babies (3 and 8 weeks) at the time of sampling. Repeat sampling of pair 6 resulted in a lower maternal 10-hydroxynortriptyline level and a nondetectable level in the infant, despite a higher maternal serum nortriptyline level. There was no evidence of accumulation of the drug or its metabolites in the infants nursed for 50 days or more (infants 3, 4, 6 [repeat sam-

ple], and 7). Although formal evaluations have not been done, the parents and pediatricians agree that these children are developing normally.

DISCUSSION

The authors of several papers (2–4) concluded that breast-feeding during amitriptyline treatment was acceptable if the risk/benefit analysis was carefully considered and the mother-infant pair was monitored. This study of nurslings whose mothers were medicated with nortriptyline revealed no detectable blood levels of nortriptyline and no adverse clinical effects. However, small amounts of the less active metabolite 10-hydroxynortriptyline were found in the sera of the two youngest infants.

It is difficult to establish a safe level of exposure to any agent. The possibility that chronic exposure to very low doses of antidepressants may affect infant neurochemical development remains a concern. Sedation and respiratory depression have been reported in a nursling whose mother was treated with doxepin (10). Metabolic variability may result in unexpectedly high serum levels in some infants.

Whether to breast-feed during antidepressant therapy is a complex decision that involves factors valued differently by women, their families, and physicians. Since

the available information does not warrant absolute recommendations, the decision must be case-specific pending further accumulation of data.

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Episode Sequence in Bipolar Disorder and Response to Lithium Treatment

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Analysis of five studies of episode sequence in bipolar disorder indicated a highly significant difference in lithium responses among sequences, favoring the mania or hypomania-depression-interval sequence over the depression-mania or hypomania-interval sequence by an odds ratio of 4.4 ($p < 0.00001$).

(Am J Psychiatry 1991; 148:1237-1239)

Suggested predictors of a good response to long-term lithium treatment in patients with bipolar disorder include family history of bipolar disorder, relatively high recurrence rate, and good interepisode recovery. Poor compliance, alcohol abuse, rapid cycling (four or more episodes per year), and episodes with mixed manic and depressive features may predict a poor response (1). Kukopulos et al. (2) proposed four bipolar disorder groups based on episode-interval sequences: mania or hypomania, followed without an interval by depression and then a euthymic interval (mania or hypomania-depression-interval); depression immediately preceding mania or hypomania, followed by an interval (depression-mania or hypomania-interval); continuous cycling, without intervals, in long or rapid cycles; or no regular sequence (irregular). They found that patients with a course of mania or hypomania-depression-interval responded best to long-term lithium treatment, while patients with depression-mania or hypomania-interval and the less common group with continuous cycling in rapid cycles responded least well (2). While several later reports seem to support these findings (3-6), some of the observations are not widely known or are individually inconclusive. Accordingly, we analyzed all

available relevant data to test the hypothesis of an association between response to lithium and episode sequence in bipolar disorder.

METHOD

Reports on this topic located by MEDLINE computer search were reviewed for comparability on the basis of subject selection, diagnosis, episode sequence, and clinical response or outcome, as summarized in table 1. Although different classifications were used, the bipolar disorder diagnosis employed similar criteria. Data first were analyzed for overall relationships among all episode sequences, lithium response rates, and studies; log-linear models were used (8). Next, we applied Fisher's exact test to obtain individual p values for the effect on lithium response of the most prevalent and consistently represented sequences (mania or hypomania-depression-interval and depression-mania or hypomania-interval); applied the Mantel-Haenszel test for homogeneity of results across studies; and obtained Mantel-Haenszel odds ratios (with Miettinen's test-based 95% confidence intervals) (7).

RESULTS

Comparable data were obtained from five studies (table 1), all using criteria for sequence typing similar to those of Kukopulos et al. (2). Ranked prevalences of 576 bipolar disorder case sequences were as follows: mania or hypomania-depression-interval; depression-mania or hypomania-interval; irregular; and continuous cycling, without intervals, in long cycles and in rapid cycles. The ranked crude rates of response to lithium were as follows: mania or hypomania-depression-interval, irregular, continuous cycling in long cycles, de-

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Supported by NIMH grants MH-31154, MH-36224, and MH-47370.

The authors thank Drs. A. Kukopulos, M. Maj, and L. Tondo for their discussions of their results and Mr. S. Ascheim for technical assistance.

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TABLE 1. Characteristics and Response to Lithium of Patients With Different Sequences of Bipolar Disorder

Study	Diagnosis	Responders ^a	Total (N=576)	Sequence ^b					
				MDI ^c (N=171)		DMI ^c (N=144)		CC-LC ^c (N=97)	
				Responders	Total	Responders	Total	Responders	Total
Kukopulos et al., 1980 (2)	Bipolar disorder (ICD-9)	No recurrences for ≥ 1 year	294	55	90	25	78	32	56
Grof et al., 1987 (3)	Bipolar disorder + bipolar-schizo- affective disorder (RDC)	No or fewer epi- sodes for ≥ 2 years	50	17	18	10	18	1	3
Haag et al., 1987 (4)	Bipolar disorder + bipolar-schizo- affective disorder (RDC)	Fewer admissions/ year for ≥ 1 year	93	26	29	10	21	3	8
Maj et al., 1989 (5)	Bipolar disorder (DSM-III)	Fewer episodes and $>50\%$ less time ill for 2 years	99	17	23	7	19	5	9
Faedda et al., 1989 (6)	Bipolar disorder, seasonal pattern (DSM-III-R)	No recurrences for ≥ 1 year	40	8	11	4	8	12	21

^aRecurrence could be full (illness similar to past history without lithium) or partial (shorter, attenuated compared to previous episodes).

^bMDI=mania or hypomania followed by depression and then a euthymic interval of 1 month or more, DMI=depression followed by mania or hypomania and then a euthymic interval of 1 month or more, CC-LC=long cycles (two or more per year) without euthymic interval, CC-RC=relatively rapid cycles (two or more per year) without euthymic interval, and IRR=irregular course with no clear sequence pattern.

^cThe MDI group represented 29.7% of the total and had a 71.9% crude response rate, the DMI group represented 25.0% of the total and had a 38.8% crude response rate, the CC-LC group represented 16.8% of the total and had a 54.6% crude response rate, the CC-RC group represented 10.8% of the total and had a 17.7% crude response rate, and the IRR group represented 17.7% of the total and had a 61.7% response rate. For the overall MDI versus DMI comparison, odds ratio=4.4 and $p<0.00001$.

^dOdds ratio was obtained by the Mantel-Haenszel method for combining 2×2 tables (7); p was obtained by Fisher's exact test (7); for response in MDI versus DMI: sensitivity=71.9% (N=123 of 171), specificity=61.1% (N=88 of 144).

^eOf 42 nonresponders, 15 later responded after antidepressants were discontinued.

pression-mania or hypomania-interval, and continuous cycling in rapid cycles. There is no evidence that there were inconsistent associations between response rates and episode sequences across studies ($\chi^2=13.4$, $df=12$, $p=0.34$). There was a highly significant overall association of response rate and episode sequence ($\chi^2=62.5$, $df=4$, $p<0.000001$); this finding was based on log-linear models for all sequences, outcomes, and studies. For responses in the most prevalent (55% of cases) and consistently reported sequences, mania or hypomania-depression-interval and depression-mania or hypomania-interval, the Mantel-Haenszel test for nonhomogeneity across studies was not significant ($\chi^2=2.58$, $df=4$, $p=0.63$), and the overall odds ratio of 4.4 (95% confidence interval=2.8–7.0) strongly favored the lithium response in the mania or hypomania-depression-interval group ($p<0.00001$).

DISCUSSION

These results support the proposal that bipolar episode sequences can predict response to lithium. While only one of the studies reviewed was prospective (5), other data (3, 4) were obtained before the formulation of a sequence hypothesis by Kukopulos et al. (2) and so evidently were acquired without bias relevant to defining the course of illness or response to treatment. However, prospective confirmatory studies are now required.

The basis of the strikingly better response in the mania-depression-interval course than in the depression-mania-interval course is uncertain. If the mania-depression-interval sequence is associated with type I bipolar disorder (manic and depressed) and the depression-mania-interval sequence with type II bipolar disorder (depressed with hypomania) (2, 6, 9), this association might bias outcome in favor of the mania-depression-interval sequence, since lithium seems more effective in preventing manic than depressive episodes (2, 10), and preventing mania may reduce risk of subsequent depression (2). Lithium response rates were 12% higher in type I bipolar disorder than in type II bipolar patients, 49.3% and 37.6%, respectively, in 253 such patients (6, 9) found ($\chi^2=3.4$, $df=1$, $p=0.06$); this result suggests a possible additional minor association of treatment response and bipolar disorder subtype (4, 6, 9). Another possibility is that the antimanic action of lithium may be more effective when euthymic intervals precede mania, in patients with the mania-depression-interval sequence, but provide less protection in patients with the depression-mania-interval sequence, since mood may switch rapidly from depression directly into mania, perhaps with added risk due to antidepressant therapy (1, 2, 10). Antidepressants also might favor a rapid cycling course and contribute to its poor lithium response (table 1) (2).

In conclusion, this summary analysis supports the proposal by Kukopulos et al. (2, 9) that episode sequence

TABLE 1 (continued)

Sequence ^b					
CC-RC ^c (N=62)		IRR ^d (N=102)		MDI Versus DMI ^d	
Responders	Total	Responders	Total	Odds Ratio	p
8	50 ^e	8	20	3.3	0.0002
—	—	9	11	13.6	0.007
—	—	22	35	9.5	0.001
3	12	24	36	4.9	0.02
—	—	—	—	2.7	0.31

can predict response to lithium in bipolar disorder. Their sequence subtyping applies to most bipolar disorder patients (2–6, 9) and may be clinically useful when sufficient history is available. Nevertheless, the sensitivity (about 72%) and specificity (about 60%) of predicting response for the mania-depression-interval sequence versus the depression-mania-interval cycle are too lim-

ited (table 1) to justify withholding treatment. Additional prospective controlled studies are needed to verify relationships between lithium response and sequences or other subtypes in bipolar disorder, to evaluate such correlations with alternative treatments (anticonvulsants), and to clarify mechanisms underlying the evidently superior response to lithium of patients with the mania-depression-interval versus depression-mania-interval sequence, including consideration of biological heterogeneity in bipolar disorder.

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Elevated Medial-Frontal Cerebral Blood Flow in Obsessive-Compulsive Patients: A SPECT Study

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Regional cerebral blood flow was measured with single photon emission computed tomography in 10 obsessive-compulsive patients and eight comparison subjects. The patients had a significantly higher ratio of medial-frontal to whole cortex blood flow; this was unrelated to symptom severity but was correlated negatively with anxiety. No differences in orbital-frontal blood flow were found.

(Am J Psychiatry 1991; 148:1240-1242)

Frontal lobe dysfunction has been implicated in obsessive-compulsive disorder. Surgical procedures that disrupt regions of the frontal lobe or projections to the frontal cortex may reduce symptoms of obsessive-compulsive disorder (1). Positron emission tomography (PET) neuroimaging studies report increased glucose metabolism in the frontal cortex of subjects with this disorder (2-5). The objective of this study was to investigate differences in frontal cortical blood flow between obsessive-compulsive patients and normal comparison subjects by means of [^{99m}Tc]d,l-hexamethylpropyleneamine oxime (HM-PAO) single photon emission computed tomography (SPECT) imaging and to determine whether such differences were correlated with measures of clinical state.

METHOD

Ten white patients who met the *DSM-III-R* criteria and the Research Diagnostic Criteria for obsessive-compulsive disorder and who gave informed consent were studied. Their mean \pm SD age was 34.1 ± 11.1 years (range=18-49 years). Their mean \pm SD educational level

was 15.5 ± 2.0 years. They were evaluated in the Johns Hopkins Hospital psychiatric outpatient department, and potential subjects were excluded if they had ever met criteria for major depression, had histories of central neurologic disorder (including head trauma leading to unconsciousness for more than 1 hour), or had histories of substance abuse. All patients had both obsessions and compulsions of varying severity; mean \pm SD Yale-Brown Obsessive Compulsive Scale (6) scores were 11.9 ± 3.1 for obsessions (range=5-15) and 12.3 ± 2.5 for compulsions (range=9-15). All but one patient had had onset of the disorder by the age of 18 years (mean \pm SD=15.8 \pm 7.7 years). One patient had transitory facial tics. Prior to the scans, all patients had been medication free for 4 weeks to 2 years.

Eight physically healthy, white, normal volunteer comparison subjects were recruited from Johns Hopkins Hospital and Johns Hopkins University employees or students and were group-matched to the patients on age, race, and sex. Their mean age was 27.5 ± 5.9 years (range=20-39 years); age differences between the groups were not statistically significant ($t=1.5$, $df=16$, $p=0.15$). The mean level of education in the comparison group was 17.6 ± 2.3 years. There were three women in each group. Potential comparison subjects were excluded from the study according to the same criteria that were used for the patients or if they had histories of any axis I psychiatric disorders.

Each of the patients with obsessive-compulsive disorder was rated clinically on the day of the scan, before injection, with the National Institute of Mental Health Global Obsessive Compulsive Scale (7), the Yale-Brown Obsessive Compulsive Scale (6), and the Hamilton Rating Scale for Anxiety (8).

For SPECT imaging, subjects received 20 mCi of [^{99m}Tc]HM-PAO (Ceretek) intravenously, 5 minutes before scanning, under resting conditions with minimal

Presented at the 143rd annual meeting of the American Psychiatric Association, New York, May 12-17, 1990. Received Aug. 7, 1990; revision received Feb. 20, 1991; accepted March 20, 1991. From the Department of Psychiatry and Behavioral Sciences and the Department of Radiology and Radiological Sciences, The Johns Hopkins Medical Institutions. Address reprint requests to Dr. Harris, Department of Psychiatry and Behavioral Sciences, Division of Psychiatric Neuroimaging, The Johns Hopkins Hospital, Meyer 3-166, 600 North Wolfe St., Baltimore, MD 21205.

Supported in part by the following grants to Dr. Pearlson: NIMH grants MH-40391 and MH-43775 and grant RR0722 from the Johns Hopkins Outpatient Clinical Research Center, NIH Division of Research Resources.

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sensory stimulation (eyes covered, in a quiet, darkened room). Studies were performed on a Toshiba GCA-90B single rotating Anger camera SPECT system with 16-mm resolution. For image analysis, transaxial, 11-mm-thick reconstructions were obtained parallel to the orbital-meatal line. Cortical circumferential profiles of radioactivity were analyzed by one of the authors (G.J.H.), blind to diagnosis, with the use of software developed in-house, on two slices: one at the level of the basal ganglia and one 1 cm above (9). The cortical circumferential profiling method uses a semiautomatic approach that defines the cortex as a ring, which is sampled contiguously by using 1-cm² samples every 6 degrees, for a total of 60 samples per slice. These samples are centered 1 cm toward the brain's geometric center from its outer edge to avoid partial volume effects. We found that the cortical circumferential profiling method greatly reduced variability of measurements, compared to manual region placement, in 15 repeated trials of each method in which we assessed values of frontal regions (variance was 9.35 with the manual method and 0.73 with profiles; $F=12.81$, $df=14, 14$, $p<0.005$).

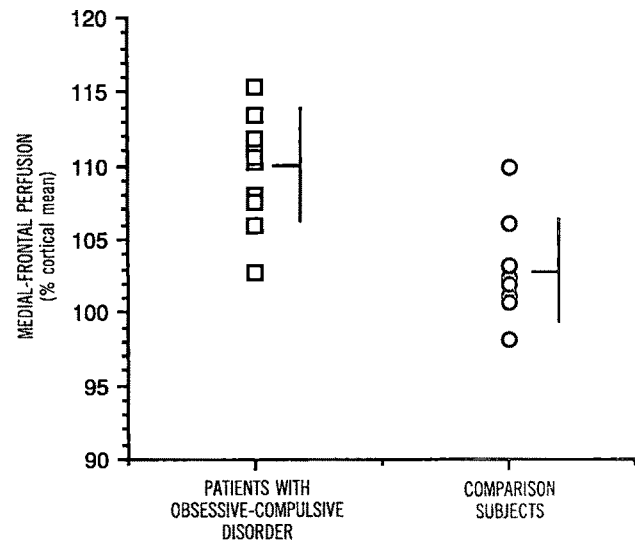
The bilateral medial-frontal cortex (e.g., the two 6-degree samples on each side of the frontal midline on both slices) was determined from the profiles. This region contains counts from the prefrontal cortex and anterior cingulate. In addition, regions corresponding to the orbital-frontal cortex were sampled by using manually placed regions of interest (1 cm²) based on the description of orbital-frontal anatomy in a study by Baxter et al. (2). Regions were expressed as percentages of the whole cortical mean value (from all 120 samples on both slices) to normalize between scans. Our regional analysis was hypothesis-driven on the basis of previous findings in frontal cortical regions (2–5). Data from other cortical regions in obsessive-compulsive disorder have been reported to be similar to control values (4, 5). Therefore, to avoid the statistical problems associated with multiple comparisons, we limited our analysis to frontal regions.

Kolmogorov-Smirnov tests indicated that all perfusion data and clinical data were normally distributed (all p values were greater than 0.75), thereby justifying the use of two-tailed t tests for comparing frontal perfusion values in the two groups. Clinical state scores were regressed on patients' perfusion values. Discriminant function analysis was performed on regions that showed significant differences.

RESULTS

The patients with obsessive-compulsive disorder had a mean \pm SD medial-frontal perfusion value of $109.7\%\pm 3.7\%$ of the cortical mean, while the comparison subjects had a value of $102.9\%\pm 3.6\%$. This difference was highly significant (figure 1). The orbital-frontal cortex, however, did not show significant differences for the left region (patients, $91.3\%\pm 7.3\%$; comparison sub-

FIGURE 1. Medial-Frontal Perfusion Values for 10 Unmedicated Patients With Obsessive-Compulsive Disorder and Eight Normal Comparison Subjects^a



^aSignificant difference between groups ($t=3.93$, $df=16$, $p=0.002$).

jects, $90.6\%\pm 5.9\%$; $t=0.23$, $df=16$, $p=0.82$) or the right region (patients, $91.3\%\pm 7.8\%$; comparison subjects, $93.3\%\pm 6.4\%$; $t=0.60$, $df=16$, $p=0.56$).

The patients' medial-frontal perfusion values demonstrated strong negative correlations with their Hamilton anxiety scores in the regression analysis ($r=-0.84$, $N=10$, $p=0.002$); this was not a result of outliers. However, the Yale-Brown obsession and compulsion scores and the global severity scores were all uncorrelated with medial-frontal perfusion ratios (each $r<0.20$, $N=10$, $p>0.50$). Values for orbital-frontal regions did not correlate with any clinical test scores. Perfusion scores were uncorrelated with age.

Discriminant function analysis based on medial-frontal values correctly identified eight (80.0%) of the 10 patients and seven (87.5%) of the eight comparison subjects, for a net discrimination of 83.3%.

DISCUSSION

Using [^{99m}Tc]HM-PAO SPECT, we found elevated medial-frontal cortical perfusion ratios, but normal orbital-frontal perfusion, in obsessive-compulsive patients. This blood flow study supports the PET study findings reported by Swedo et al. (5), who found increased prefrontal and anterior cingulate metabolism. Our results agree with earlier PET studies (3, 5) that reported no correlation between frontal function and obsession-compulsion scale scores. Our findings differ from those of PET studies using one-tailed t tests (2, 4) that found increased orbital-frontal glucose metabolism in obsessive-compulsive disorder. One explanation for our negative finding for orbital-frontal metabolism may be that our study was at a methodological disad-

vantage compared to PET studies because of our thicker slices and lower resolution. These made locating the orbital-frontal cortex more difficult. Baxter et al. (2) also had difficulty in locating this region on some scans. Our results indicate that the medial-frontal regions have a more robust difference in blood flow than the orbital-frontal regions in obsessive-compulsive disorder, as was also reported by Swedo et al. (5).

We initially suspected that our finding might be due to scan-related anxiety in the patients. However, we found that the more anxious patients had relatively lower medial-frontal perfusion ratios. This finding of an inverse relation between cerebral perfusion and anxiety state at relatively high levels of anxiety is in agreement with results reported by Gur et al. (10), although their study was based on absolute values. Our finding of increased medial-frontal perfusion in patients with obsessive-compulsive disorder is consistent with the hypothesis of frontal lobe involvement in this disorder.

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Effects of Fluoxetine on Regional Cerebral Blood Flow in Obsessive-Compulsive Patients

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Six drug-free obsessive-compulsive patients were given single photon emission computerized tomography scans before and during treatment with fluoxetine. The treatment significantly reduced the patients' "hyperfrontality," as determined by the ratio between medial-frontal and whole cerebral cortex blood flow, and significantly lowered ratings of obsessive-compulsive and anxiety symptoms.

(Am J Psychiatry 1991; 148:1243-1245)

Several studies have found that patients with obsessive-compulsive disorder show heightened glucose metabolism in frontal (primarily orbital-frontal) brain areas (1-4). We report in another article in this issue (5) that these patients exhibit increased blood flow in the medial-frontal cortex. If this observed "hyperfrontality" is associated with obsessive-compulsive pathology, one would expect that a significant reduction of obsessive-compulsive symptoms would be accompanied by concomitant decreases in frontal cerebral blood flow (CBF). A decrease of glucose metabolism in the orbital-frontal and left caudate region has been reported in obsessive-compulsive patients receiving clomipramine treatment (2). In this study we used single photon emission computed tomography (SPECT) to examine the effect of fluoxetine treatment on regional CBF in patients with obsessive-compulsive disorder. Fluoxetine, which has been found to be effective in the treatment of obsessive-compulsive disorder (6), was chosen because it is a pharmacologically "cleaner" serotonin reuptake blocker than clomipramine.

METHOD

Six patients, given diagnoses of obsessive-compulsive disorder according to *DSM-III-R*, participated in the

study. They had been free of drugs affecting the CNS for at least 1 month. All gave informed consent. Their mean \pm SD age was 33.3 \pm 9.8 years (range=19-42 years). Three of the patients were male, all were white, and their mean \pm SD educational level was 16 \pm 2.7 years (12th grade to doctoral degree). The mean age at onset of obsessive-compulsive disorder was 15.3 \pm 2.2 years (range=13-18 years). At the time of the study none of the patients suffered additional psychiatric or physical illnesses, except for generalized anxiety in four patients and transitory facial tics in one patient. All patients had normal brain magnetic resonance imaging scans.

The patients were assessed by the same psychiatrists on the days of the first and second scans with the National Institute of Mental Health Global Obsessive Compulsive Scale (7) and the Yale-Brown Obsessive Compulsive Scale (8) to measure obsessive-compulsive symptoms and the Hamilton Rating Scale for Anxiety (9) to measure anxiety symptoms.

Following their first SPECT scans, the patients were placed on a regimen of fluoxetine, 20 mg/day. This dosage was increased by 20 mg every week, or more slowly if there were side effects, to reach a daily dose of 80-100 mg of fluoxetine. Five patients had their second scans after 4 months of treatment and one after 3 months of treatment. Five patients received 80 mg/day and one 100 mg/day of fluoxetine for at least the month before their second scans. The patients took no other medications.

The regional CBF studies were done according to the method described in our other article in this issue (5). Normalized frontal perfusion values were compared by using two-tailed *t* tests. In addition, they were correlated with clinical measures by means of regression analysis.

RESULTS

Table 1 and figure 1 show that during fluoxetine treatment, the ratio of medial-frontal to whole corti-

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Supported in part by the following grants to Dr. Pearlson: NIMH grants MH-40391 and MH-43775 and grant RR0722 from the Johns Hopkins Outpatient Clinical Research Center, NIH Division of Research Resources.

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TABLE 1. Regional Cerebral Blood Flow and Clinical Ratings of Six Patients With Obsessive-Compulsive Disorder Before and During Treatment With Fluoxetine

Measure	Baseline		During Fluoxetine Treatment		t^a (df=5)	p
	Mean	SD	Mean	SD		
Regional cerebral blood flow ^b						
Medial-frontal	109.4	2.77	105.0	3.98	3.65	<0.02
Right orbital-frontal	90.8	7.90	90.3	5.30	0.15	n.s.
Left orbital-frontal	90.7	7.40	93.4	3.80	1.08	n.s.
NIMH obsessive compulsive scale score	9.0	1.14	5.5	1.01	3.66	<0.02
Yale-Brown Obsessive Compulsive Scale score	23.8	4.44	12.5	5.24	3.41	<0.02
Hamilton anxiety scale score	20.0	9.94	7.8	4.70	3.10	<0.03

^aPaired two-tailed test.

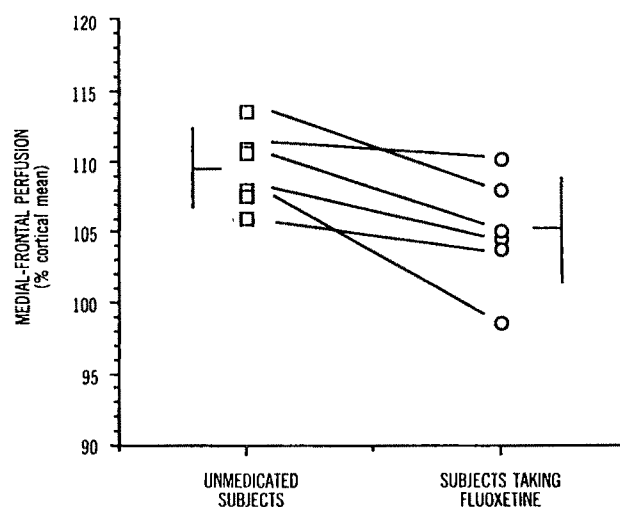
^bExpressed as percentage of mean cortical value. We found the following regional cerebral blood flow values in eight normal subjects: medial-frontal, 102.9%±3.6%; right orbital-frontal, 93.3%±6.4%; left orbital-frontal, 90.6%±5.9% (5).

cal CBF decreased significantly, approaching values seen in normal subjects. Concomitantly, clinical ratings on the two scales measuring obsessive-compulsive symptoms and the scale of anxiety symptoms decreased significantly. Correlations between medial-frontal regional CBF ratio and clinical ratings before and during treatment were not significant (each $r < 0.20$, $N=6$, $p > 0.50$), except for a negative correlation between the medial-frontal ratio and the ratings on the Hamilton anxiety scale before treatment ($r = -0.88$, $N=6$, $p < 0.01$). Correlations between changes in medial-frontal to whole cortex regional CBF ratio and changes in clinical ratings did not reach significance. As noted in our previous study (5), the ratio of orbital-frontal segments to the whole cerebral cortex was similar in patients and normal comparison subjects, and it did not change significantly when the patients were taking fluoxetine. Correlations of orbital-frontal ratio and clinical ratings were not significant.

DISCUSSION

When treated with fluoxetine, our obsessive-compulsive patients, as a group, showed a significant decrease in their medial-frontal regional CBF ratio as well as a decrease of obsessive-compulsive and anxiety symptoms. The medial-frontal and orbital-frontal regional CBF ratios were uncorrelated with obsessive-compulsive symptoms before and during treatment. The inverse correlation between anxiety and medial-frontal regional CBF ratio in untreated obsessive-compulsive patients is reported and discussed in our other article in this issue (5). Differences between our findings and those of Benkelfat et al. (2) need to be investigated. They could be attributable to differences between the investigated medications, the scanning techniques, or the selection of patients.

The observed decrease in medial-frontal regional CBF ratio during fluoxetine treatment could be associated with a specific therapeutic effect of the drug in

FIGURE 1. Medial-Frontal Perfusion Values for Six Patients With Obsessive-Compulsive Disorder Before and During Treatment With Fluoxetine^a

^aLines between groups connect measures for the same subject. The group difference was significant ($t=3.65$, $df=5$, $p < 0.02$).

obsessive-compulsive disorder. Alternatively, decreases in the medial-frontal regional CBF ratio may be a nonspecific effect of fluoxetine treatment unrelated to the underlying disorder. In this case, patients with other diagnoses should show similar changes when treated with fluoxetine. An alternative explanation was suggested by Baxter et al. (10), namely, that decreases in cerebral metabolism and blood flow may be associated with decreases in obsessive-compulsive symptoms irrespective of the type of treatment. If so, successful behavior therapy and pharmacotherapy should yield similar results. Finally, hyperfrontality could be related to patients' attempts to suppress compulsions during scanning and represent a nonspecific, reversible, compensatory effect for the illness. Further studies are necessary to improve our understanding of the relation between regional CBF and clinical symptoms in obsessive-compulsive disorder.

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Plasma Homovanillic Acid in Schizotypal Personality Disorder

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Schizotypal patients were found to have a significantly higher mean plasma HVA concentration than normal comparison subjects. Furthermore, plasma HVA concentration positively correlated with "psychotic-like" schizotypal symptoms. These results implicate dopaminergic mechanisms modulating the psychotic-like symptoms of schizotypal personality disorder.
(Am J Psychiatry 1991; 148:1246-1248)

Schizotypal personality disorder is closely related to schizophrenia in its phenomenology (1), genetics (2), biology (3), and response to treatment (4). Like chronic schizophrenic patients, patients with schizotypal personality disorder exhibit both "psychotic-like" symptoms—e.g., ideas of reference, cognitive/perceptual distortions, and suspiciousness—and other symptoms more reflective of social deficit, e.g., social isolation and inadequate rapport (1). Eye movement dysfunction and other attentional measures are associated particularly with the social deficit symptoms of schizotypal personality disorder (3, 5), whereas correlates of the psychotic-like symptoms have yet to be established. However, the psychotic-like symptoms of schizotypal personality disorder are reduced by neuroleptic treatment (4), as in schizophrenia, implicating dopaminergic modulation of these symptoms. Plasma concentrations of the major dopamine metabolite homovanillic acid (HVA), a possible index of brain dopamine neuronal activity (6), have been shown to correlate with the psychotic symptoms of schizophrenia (7-9). Thus, it was hypothesized that plasma HVA concentrations would correlate with the psychotic-like symptoms of schizotypal personality disorder. To test this hypothesis, plasma HVA concentrations were studied in patients with schizotypal personality disorder

and two comparison groups: normal volunteers and patients with other personality disorders.

METHOD

The subjects were 11 male patients with schizotypal personality disorder; five men and two women with personality disorders other than schizotypal, paranoid, and schizoid; and six male normal comparison subjects. All gave informed consent after the study procedures were explained to them. Each of the normal comparison subjects was determined to be free of a personal history and a family history of *DSM-III* axis I disorders and of a personal history of *DSM-III* axis II disorders by a research psychiatrist (E.F.C.) using a clinical interview with a *DSM-III* checklist for axis I and axis II disorders. The axis I diagnoses for all personality disorder patients were derived from interviews with patients and informants close to the patient by raters using the Schedule for Affective Disorders and Schizophrenia (10); the interrater reliability (kappa) for schizophrenia was 0.80, and for major affective disorders it was 0.87. The axis II diagnoses were based on the Structured Interview for the *DSM-III* Personality Disorders (11), as described elsewhere (5); the interrater reliability kappa for schizotypal personality disorder in our laboratory is 0.73. The *DSM-III* schizotypal personality disorder symptoms were assessed with the Structured Interview for the *DSM-III* Personality Disorders. The *DSM-III* schizotypal personality disorder symptoms of magical thinking, ideas of reference, recurrent illusions, and suspiciousness were considered as the psychotic-like symptoms because of their phenomenological similarity to the psychotic symptoms of schizophrenia. Four patients with schizotypal personality disorder and four patients with other personality disorders also met the *DSM-III* criteria for current major depressive episode. Five patients with schizotypal personality disorder and three

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The authors thank Robert Trestman, M.D., Theresa Mahon, M.A., Felice Ramallah, M.A., Clarence Leung, B.A., Vivian Mitropoulos, M.A., James Weissberg, M.A., Melissa Kresch, M.A., and Chris Kasoupis, M.A., for their contributions to this study.

Supported in part by VA Merit Reviews 7609-001 and 7609-014 to Dr. Siever and by the Bronx VA Schizophrenia Biologic Research Center.

patients with other personality disorders also met the criteria for *DSM-III* borderline personality disorder.

All subjects were found to be free of medical illnesses in physical and laboratory examinations. None of the patients had used any psychotropic medication for at least 2 weeks before the study. The subjects were instructed to ingest a low-monoamine diet for 72 hours before the study, fasted overnight, avoided strenuous physical activity that morning, and arrived at 8:00 a.m. The subjects were not allowed to smoke immediately before and during the test. An intravenous line was started at 9:00 a.m. At 9:55 a.m., a 5-ml blood sample was obtained; it was processed, stored, and assayed for HVA by means of gas chromatography/mass spectrometry (intra- and interassay coefficients of variation, 4.6% and 8.6%, respectively), as described elsewhere (9). Data analysis was performed with analysis of variance (ANOVA), Tukey multiple comparison test, and Pearson correlation coefficient, as appropriate.

RESULTS

The mean \pm SD plasma HVA concentration of the schizotypal personality disorder group (12.9 ± 4.60 ng/ml) was compared with the concentrations of the patients with other personality disorders (9.1 ± 2.53 ng/ml) and the normal comparison group (7.8 ± 1.30 ng/ml) by means of ANOVA ($F=4.85$, $df=2, 21$, $p<0.02$). The schizotypal personality disorder group had a significantly higher plasma HVA concentration than the normal comparison group (Tukey $p<0.05$), but the plasma HVA concentration of the group with other personality disorders did not significantly differ from that of either of the other two groups. These statistically significant differences were not related to either differences in gender or presence or absence of major depression. No significant difference in plasma HVA concentration was found between the subjects with schizotypal personality disorder who were either never treated with neuroleptics or were treated more than 90 days before the study ($N=7$, plasma HVA= 12.6 ± 5.7) and those treated within 90 days of the study ($N=4$, plasma HVA= 13.4 ± 2.1) ($t=-0.27$, $df=9$, $p=0.8$).

The mean plasma HVA concentration of the schizotypal personality group was also found to be significantly higher than the 10:00 a.m. concentration of another group of 14 male normal comparison subjects (8.8 ± 2.6 ng/ml) ($t=2.77$, $df=23$, $p<0.01$) studied at this research center at the end of an overnight, but otherwise methodologically identical, study (9).

The relationship of plasma HVA concentration to the severity of psychotic-like symptoms was then examined. Since psychotic-like symptoms of schizotypal personality disorder are present not only in patients with schizotypal personality disorder but in patients with other personality disorders as well, all personality disorder patients were examined together. The normal comparison subjects were excluded from this analysis. In the total group of personality disorder patients

($N=18$), plasma HVA concentration correlated significantly with the number of psychotic-like schizotypal personality disorder criteria in each patient ($r=0.61$, $df=16$, two tailed $p=0.007$). The number of other schizotypal personality disorder criteria did not correlate with plasma HVA concentration ($r=0.20$, $df=16$, $p=0.4$).

DISCUSSION

The main findings of this study were 1) the mean plasma HVA concentration of patients with schizotypal personality disorder was significantly higher than that of normal comparison subjects and 2) plasma HVA concentration correlated positively with the number of psychotic-like *DSM-III* schizotypal personality disorder criteria.

The CSF concentrations of HVA in an overlapping sample of patients with schizotypal personality disorder were also higher than those of a group of patients with other personality disorders and correlated significantly with psychotic-like symptoms of schizotypal personality disorder in a preliminary report (12) and a recent update of this ongoing study (Siever et al., unpublished report, 1990).

Although a portion of HVA in plasma is derived from the brain, a significant amount is contributed by the peripheral dopamine metabolism (6–9), so the correlation of plasma HVA concentration with the psychotic-like schizotypal personality disorder symptoms might be attributable to variations in the peripheral HVA contributions. However, the similar correlation of the psychotic-like symptoms of schizotypal personality disorder with CSF HVA concentration raises the possibility these associations might be attributable to variations in central dopaminergic activity.

These findings suggest dopaminergic mechanisms underlying the psychotic-like symptoms of schizotypal personality disorder and support the concept that the psychotic-like symptoms of schizotypal personality disorder and psychotic symptoms of schizophrenia are not only phenomenologically similar but are biologically related as well. Because of the small number of subjects, the findings of this report must be regarded as preliminary. However, if such associations between the psychotic-like symptoms of schizotypal personality disorder and plasma/CSF HVA concentrations are replicated with larger groups, it would suggest that a higher than normal plasma HVA concentration may be a biological correlate of the psychotic symptoms of the schizophrenia spectrum.

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Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

TEXTBOOKS AND GUIDES

Psychiatry for Medical Students, 2nd ed., by Robert J. Waldinger, M.D. Washington, D.C., American Psychiatric Press, 1990, 590 pp., \$49.95; \$35.00 (paper).

This book is a simple, easy to read, well-designed, and logical approach to psychiatry for the average student. It begins with a segment on assessment skills that assists the student in understanding what is necessary to take a psychiatric history and perform an adequate mental status examination. This portion of the book has multiple examples, including concrete questions that should help students acquire mastery of the basic skills of interviewing. This section is followed by an introduction to psychopathology that focuses on the major psychiatric disorders without completely rewriting *DSM-III-R*. The third and fourth sections of the book are devoted to special populations such as the elderly, children, and medically ill patients as well as special problems in psychiatry, including sexuality, substance abuse, eating disorders, suicide, and violence. The final section of the book reviews treatment strategies and addresses outpatient modalities such as different psychotherapies, somatic treatments, ECT, and group, couple, and family treatment. There is no general discussion of inpatient management or the indications for hospitalization.

This book is particularly good for beginning students in several areas. The section on human sexuality, in addition to reviewing the sexual dysfunctions, provides a comprehensive outline for taking a sexual history along with examples of what to say. There is also a brief discussion of how one's own attitudes about sexuality may affect the history-taking process. The section on personality disorders is helpful, not only because it provides lists of *DSM-III-R* phenomenological criteria but especially because it supplies an overview of "character" and evocative descriptions of personality types with pertinent discussions of treatment options.

The summary of treatment modalities is comprehensive and includes a discussion of cognitive and behavioral treatments in addition to the more "traditional" analytic psychotherapies. The review of somatic treatments is excellent, especially with regard to the side effects and prescribing of antidepressants and benzodiazepines. Somewhat misleading, however, is a section that lists depressive symptoms and suggests that certain symptoms are more likely to respond to medication than others. Furthermore, categorizing entities such as dysthymic disorder or personality disorders as not likely to respond to medication may heighten the student's tendency to reach premature and possibly erroneous conclusions.

One surprising omission from this book, given its scope, is the lack of a section on AIDS and HIV disease in psychiatric practice. The beginning student needs to understand the psychiatric manifestations of AIDS, the impact of HIV infection on the individual patient, its consequences for those already at risk for psychiatric disease, AIDS anxiety in the "worried well," the significance of sexual practices and behaviors in the

spread of AIDS, and the role of the psychiatrist in the ethical issues that may arise in treating patients who are HIV positive.

Overall, however, this book is a welcome addition to the literature available to beginning medical students. It is particularly useful for courses in which the focus is on the teaching of psychiatry as opposed to courses teaching "human behavior," where the educational emphasis is on the teaching of psychiatric principles for use by nonpsychiatric physicians.

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The Healing Brain: A Scientific Reader, edited by Robert E. Ornstein and Charles Swencionis. New York, Guilford Press, 1990, 262 pp., \$25.95; \$17.95 (paper).

I have long been a Robert Ornstein fan. I thought *Healthy Pleasures* (1) an especially good read. In 1985 I attended a 2-day workshop entitled "The Healing Brain" conducted by Ornstein and David Sobel. Needless to say, it was with great delight that I approached the task of reviewing this book. I anticipated finding state-of-the-art research that would assist me in staying up-to-date.

This book contains 20 different chapters on a range of topics authored by almost as many different authors. All are relevant to the healing brain and brain function. Although the chapter titles seemed pertinent, I found most of the discussion and findings outdated. Nine of the chapters are reprints of articles that appeared elsewhere. Two of the articles predate 1980, and all but one of the remainder predate 1986. I did not find very many current books or articles in the reference sections of the other papers, either. I definitely do not agree with the statement on the book's flyer attributed to another reviewer that this book provides an excellent overview of the current status of mind-body research. I found very little in this book that I did not already know from other sources. I also found it disconcerting from the point of view of this review that I could summarize the meat of each chapter in one sentence.

By way of a conclusion, I would say that this book may be of value to a lay person or a new professional in this field. It is of value to a sophisticated and knowledgeable clinician or researcher in the field only in summarizing the basics of what is known. The reader might even be frustrated by wanting to hurry along to get to something that is not reasonably common knowledge.

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Textbook of Child Neurology, 4th ed., by John H. Menkes, M.D. Philadelphia, Lea & Febiger, 1990, 796 pp., \$78.00.

This is an excellent book. Since its first edition in 1974, it has been regarded as a preeminent text. The fourth edition continues this high standard; it reflects recent advances in the areas of neuroimaging and molecular biology. In doing so, it makes valuable new information accessible to child psychiatrists, especially those of us who trained in "pre-revolutionary" times. Accessibility is a hallmark of this book. Its physical form is well done: typefaces, headings, photographs, and diagrams all contribute to a clear and enjoyable presentation. In this age of multiauthored texts, the bulk of this book is written by Dr. Menkes himself, and he writes very well.

The chapter structure is effective. The book begins with an introduction focusing on the neurological evaluation of the child and infant, which we predict will become a standard. Subsequent chapters address specific disease entities. A long (101 pages) chapter on metabolic diseases of the nervous system is a paradigm. It begins with a section on laboratory assessment. This helps organize the reader's response to this area, which many of us may find confusing and daunting. The rest of the chapter is concise yet detailed enough to present useful information about each condition. The book covers the full range of neurological diseases in children. When we examined somewhat familiar areas, such as Tourette syndrome and developmental disorders, we found sections sufficiently complete and that present information we consider important to our colleagues. Each chapter stands well on its own and can be read without reference to the others. The section on paroxysmal disorders provides clinical descriptions useful for differential diagnosis, along with recent advances including positron emission tomography scanning. The chapter on disorders of mental development, by Marcel Kinsbourne, is a well-written practical introduction to this area for the general psychiatrist. The child psychiatrist will desire more detail, as is found in more specialized texts, but could use this section as a reference for other professionals or parents, especially in regard to language and learning disorders.

In general, this book will be a useful reference to all child psychiatrists and is worth purchasing by anyone seeing medically ill children. Menkes's text is a standard for our neurological colleagues and residents.

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The Essential Guide to Psychiatric Drugs, by Jack M. Gorman, M.D. New York, St. Martin's Press, 1990, 389 pp., \$22.95.

The Essential Guide is neither a condensed version of *Physician's Desk Reference* nor just another mini-text of psychiatry for patients. Rather, it combines features of both in presenting an approach to understanding psychiatric disorders that is both novel and worthwhile.

Dr. Gorman is well informed and writes well, two indispensable ingredients for any successful book for the lay reader. In addition, he is well organized. He gives us what patients need to know about drugs in three doses.

A 40-page introductory section presents an overview of what any patient (or relative) needs to recognize psychiatric symptoms and to find the appropriate therapist. Dr. Gorman carefully points out that having a psychiatric disorder does not

necessarily demand drug treatment. This is a viewpoint you will not find in *Physician's Desk Reference*.

Most of the book—more than 250 pages—is devoted to descriptions of the principal psychiatric disorders and the drugs used to treat them. This section is attractively laid out and printed on gray paper with plenty of boxes for easy reference; the comparison with *DSM-III-R* is compelling. The chapter on depression, for example, begins with descriptions of the main types of depression, then proceeds to a clear, careful, comprehensive description of the major antidepressants. Each drug is listed with brand name, indications, contraindications, recommended laboratory tests, common and uncommon side effects and what to do about them, usual dose, and cost. The use of ECT is summarized in 4 pages. This section of the book also includes chapters on drugs used to treat anxiety, bipolar disorder, and schizophrenia as well as sleeping pills and drugs used to treat substance abuse.

Several special topics are discussed in the third major section: treating the violent patient, etiology, weight change, sex, the elderly, pregnancy, AIDS, generics, and a brief chapter on how drugs work.

The disorder-oriented format of the main section causes some difficulty in presenting uncommon uses of psychotropic drugs. The reader will not learn about using thioridazine for premature ejaculation, for example. Treatment of jet lag with hypnotics is discussed in half a page; Dr. Gorman waffles, but in the end he recommends against the practice on the grounds that jet lag is not an illness. This may be news for the victim of an intercontinental red-eye flight. However, the patient with anorexia nervosa, agoraphobia, or obsessive-compulsive disorder can find information in this book that may help in choosing (or rejecting) drug therapy.

Of all the hazards lying athwart the successful treatment of psychiatric disorders, perhaps the worst is an uninformed patient. *The Essential Guide* goes a long way toward turning the patient into a strong, participating member of the health care team.

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Lithium and Manic Depression: A Guide, revised ed., by John Bohn and James W. Jefferson. Madison, Lithium Information Center, University of Wisconsin, 1990, 28 pp., \$4.95 (paper).

Carbamazepine and Manic-Depression: A Guide, by Janet R. Medenwald. Madison, Lithium Information Center, University of Wisconsin, 1988, 32 pp., \$4.95 (paper).

Obsessive Compulsive Disorder: A Guide, by John H. Greist. Madison, Anxiety Disorders Center, University of Wisconsin, 1989, 45 pp., \$4.95 (paper).

Electroconvulsive Therapy: A Guide, by David C. Dries and Nancy E. Barklage. Madison, Center for Affective Disorders and Lithium Information, University of Wisconsin, 1989, 17 pp., \$3.50 (paper).

These manuals were written as informational sources for patients being treated with the modalities in their titles, as well as for "families, friends, or others interested in learning" about these topics. The manuals are being reviewed together because their formats are essentially identical.

The manuals concerning specific treatment modalities (ECT, lithium, carbamazepine) introduce their topics with a

brief historical overview of their discovery or use. Following their introductions, the manuals address such topics as the frequency, heritability, and postulated etiology of obsessive-compulsive disorder, depression, and mania. The obsessive-compulsive disorder manual begins by describing obsessions and compulsions and gives two case vignettes. All of the manuals discuss what to expect when starting treatment, side effects of treatment, laboratory tests necessitated by treatment, and the role of psychotherapy. Finally, the manuals review practical questions regarding such topics as alcohol use, special diets, addiction potential, oral contraceptive use, and what to do if doses are missed.

The manual covering obsessive-compulsive disorder is by far the most comprehensive. In addition to the material contained in all of the manuals, it includes an example of an obsessive-compulsive checklist and discusses behavior therapy, pharmacological therapy, ECT, and psychosurgery as they apply to obsessive-compulsive disorder. This manual suffers somewhat from being dated. Since its publication, clomipramine has become available for prescription in the United States. Thus, the lack of relevance of reference to this drug as being available only experimentally and how to gain access to programs using it would have to be explained to patients before distribution.

Overall, I felt that these manuals could be a useful source of information for patients. They are easy to read, contain practical information, and would ease to some degree the physician's burden of providing such information. However, except for the one on obsessive-compulsive disorder, these manuals contain less information about the specific illness for which the treatments are generally intended than they do regarding side effects and laboratory studies and thus do not fill this informational void. With this latter reservation in mind, I still recommend considering their use.

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PSYCHOPHARMACOLOGY

Ecstasy: The Clinical, Pharmacological and Neurotoxicological Effects, edited by Stephen J. Peroutka. Dordrecht, The Netherlands, Kluwer Academic, 1989, 239 pp., \$87.95.

In an age when fulsome odors emerging from unsolicited magazines and newspaper supplements proclaim a copyrighted relationship to states of passion, joy, or intimacy, it should not be surprising that 3,4-methylenedioxymethamphetamine (MDMA), a drug which might destroy serotonergic neurons in the medulla, is marketed on the street under the name "ecstasy." Whether neurotoxicity is a predictable result of recreational use of this drug is an important investigative and clinical issue, as is whether the phenomenology induced deserves a name evoking the experiences of William James and Saint Teresa of Avila. Its other popular name, Adam, an anagram coined by a psychologist, is only superficially more modest. The disparity between the available animal and human data, and between knowledge and belief, is remarkable for an agent patented in 1914 with a current usage, in some urban areas, as high as 30,000 doses a month. The evidence to date would indicate that MDMA is substantially different from other recreational drugs in its pattern of self-administration, its inter-species pharmacology, and its cumulative effects over time. Several authors have suggested the

term "entactogen" ("inner touching") to denote the special qualities of MDMA and related drugs.

This book, which surveys the bumpy terrain of the effects of MDMA, is as unique as the drug itself. It contains chapters by basic neuroscientists demonstrating the effect of repeated systemic administration of MDMA on the density of 5-HT uptake sites in different brain regions and chapters by psychotherapists providing clinical vignettes of the positive effects of drug-induced psychotherapy sessions. Unfortunately, it is unlikely that any therapeutic benefit, if it exists, will ever be demonstrated scientifically because of MDMA's placement in Schedule I by the Drug and Food Administration and its status as an uncertified "orphan" drug. The influence of its orphan status may not be insignificant, given the rather different developmental history of fenfluramine, a widely prescribed and approved anorectic agent, which produces serotonergic changes similar to those of MDMA at doses quite close to those used therapeutically. Fenfluramine, however, is in Schedule IV, and there is no specific mention of its potential neurotoxic effects in *Physician's Desk Reference*.

For a slim, rapidly published work surveying a confusing and shifting literature in neuroscience, epidemiology, psychotherapy, and government legislation, *Ecstasy*, the book, is a marvel—fair to differing viewpoints, crisply edited, extensively referenced, and historically wise. Predictably, the anecdotal clinical reports suffer in comparison with the animal investigations, leaving open the questions of selection bias and long-term assessment of benefits and cost. It is possible that neurotoxicological effects could be divorced from psychopharmacological response in a new analog compound or with the addition of adjunctive agents. Several contributors found that fluoxetine has some efficacy in this regard. Regardless of the social or neurochemical course MDMA research takes, however, it will be some time before this scholarly summary is surpassed.

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Benzodiazepine Dependence, Toxicity, and Abuse: A Task Force Report of the American Psychiatric Association. Washington, D.C., APA, 1990, 108 pp., \$25.00.

Benzodiazepines are one of the most widely prescribed classes of medications by psychiatrists and nonpsychiatrists alike: approximately 11% of the adult population have taken an anxiolytic one or more times during the previous year. With the advent of newer, more specific uses of benzodiazepines in psychiatry (e.g., bipolar illness and schizophrenia) as well as the dependency and toxicity syndromes that psychiatrists are often asked to evaluate and manage, this text comes at an important time. Following the tradition of task force reports of the American Psychiatric Association, this book is a clinical guide to the rational use of these medications. It is short and concise. Readers can get through the book in an afternoon and feel as though they had attended grand rounds.

The 11 chapters are well written; instead of contributions varying in style and level of sophistication, there is a sense that editorial control was used. The initial chapter on clinical pharmacology highlights the basic and clinically useful aspects of benzodiazepine pharmacokinetics. In "Patterns of Benzodiazepine Use," four groups of long-term regular benzodiazepine users are identified: patients with medical illnesses, dysthymic patients, panic patients, and schizophrenic patients. In the chapters discussing the physiological nature of

dependence and withdrawal, lists of drug and patient characteristics as well as symptoms of dependency and withdrawal are so complete they can be used as checklists in the evaluation of patients.

Although the chapter on the mechanism of benzodiazepine dependence and tolerance is the shortest (about one and a half pages), it is technically sophisticated and complete. It might even be useful to patients trying to understand their condition. Also, because the signs and symptoms of withdrawal and toxicity vary widely, many nonpsychiatric clinicians could benefit from reading about how these syndromes present in patients.

The chapter on liability focuses on the abuse potential of benzodiazepines, but no information is provided on the liability of physicians who prescribe these medications. The prescribing of medications is a complex and often psychodynamically rich event. Especially when prescribing potentially addictive medications, physicians need to be aware of how clinical and forensic issues interact (1). Additionally, no mention is made of using tricyclic antidepressants in helping panic patients avoid suffering from insomnia and dysphoria while they taper and discontinue use of benzodiazepines (2).

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RONALD J. KOSHES, M.D.
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The Neuroleptic-Nonresponsive Patient: Characterization and Treatment, edited by Burt Angrist, M.D., and S. Charles Schulz, M.D. Washington, D.C., American Psychiatric Press, 1990, 164 pp., \$22.50.

The time for a more realistic assessment of treatment outcomes in schizophrenia is nearing. The 1970s focused on the affective disorders and neglected schizophrenia, but the 1990s have yet to become the decade of schizophrenia. The chronically mentally ill have become the worthy object of clinical research scrutiny. Not that we understand schizophrenia better than we do affective disorders, but there is a change in climate that started with unsuccessful attempts in the late 1970s to use hemodialysis and propranolol to treat patients with chronic schizophrenia. These studies highlighted the need for good treatment research in schizophrenia.

The title of this book promises to tell the reader how to identify and treat the patient who does not respond to neuroleptics. After everything is said and done, however, the patient who does not respond to neuroleptics remains. It becomes clear that it is not so easy to define the nonresponding patient and that most patients are only partial responders. The contributors direct their attention to how to reach those patients who can be helped with our present-day knowledge. The real nonresponders or partial responders will still be waiting in the wings for newer developments. What the book gives us is rational psychopharmacotherapy—prescribing practices to optimize the antipsychotic power of our psychotherapeutic agents. Although unsatisfactory in many instances, they are still among the most potent treatments in medicine.

The book brings together many important advances and hard-won treatment concepts developed over the last few

years. It tries to explode the persistent myths that all patients would respond if only they were compliant, that the antipsychotic response is immediate and fast, and that more of an antipsychotic drug is better. Interestingly, the use of multiple antipsychotic drugs together is not mentioned, as if that ill-behotten practice had been eradicated.

In our present-day practice, where length of observation and treatment is dictated by third-party payers and billing departments, it is difficult for clinicians to develop independently useful prescribing practices. It is important that information gathered by seasoned clinicians and clinical researchers be shared with a broader public. It is often forgotten that in 1980 John Davis et al. (1) summarized the ample evidence that 500 to 1000 mg of chlorpromazine equivalents, or 10 to 20 mg of haloperidol, is enough for most psychotic patients and that megadoses, if anything, do not enhance rate of response.

The book progresses from the attempt to identify the neuroleptic nonresponder clinically and biochemically to a focus on how optimally and rationally to treat schizophrenic patients with the available antipsychotic drugs. The authors also discuss augmentation therapy as well as the promising antipsychotic agent clozapine, which has recently become available in the United States.

The chapter by Richard Keefe et al. attempts to delineate clinically the treatment refractory or poorly responsive patient. The authors point out that in all likelihood we are not dealing with a different subtype but the end of a spectrum of severity. The more dimensions of poor prognosis are present in a given patient, the worse the outcome is. Although heterogeneity in course, outcome, and treatment response intuitively suggests heterogeneity in etiology, bad schizophrenia remains bad schizophrenia, even though some patients may become less psychotic after the first 10 years of illness. We will have to wait for etiologically more meaningful subdivisions than drug response and outcome. Malcolm Bowers, the father of spinal fluid monoamine studies in schizophrenia in the United States, reviews his work and that of others on how the pre-treatment biochemical state and the biochemical response to antipsychotics may help us to define the drug-nonresponsive patient. To define the patient who responds to treatment, however, is less elusive. Drug response seems to depend on the ability of the dopamine and noradrenergic systems to respond and adapt to the pharmacological interventions.

Certain principles of pharmacological treatment of schizophrenic patients are spelled out: 1) Time is needed for an antipsychotic drug to work. 2) Although the chaotic environment of an admission unit is obviously the wrong place for acutely psychotic patients, psychotic patients need time to recover. 3) Time-pressured psychiatrists may increase the dose too much too fast. 4) When patients finally do improve, sometimes after a switch in neuroleptic, the clinician will be hard pressed not to believe that the response indicates that the right dose and neuroleptic have been given. As Theodore Van Putten et al. point out, lowering the dose may lead to further improvement if side effects or excessive dopamine blockade in the striatum interferes with information processing in the corticostriatal complex. Van Putten et al. bring clarity to the elusive concept of the therapeutic window, at least for haloperidol, and review the neuroleptic blood level literature. Adam Wolkin et al. back up the low-dose concept of neuroleptic treatment by showing that 85% of central D₂ receptors are blocked with 10 mg of haloperidol, if indeed the therapeutic action of these drugs takes place at this site. The data presented by Bowers suggest that dopamine and norepinephrine levels at the receptor site may play a role as well. The positron emission data of Wolkin et al. indicate that D₂ receptor occupancy

is similar for neuroleptic responders and nonresponders, which suggests that processes beyond the receptor molecule itself may determine drug response.

The next set of chapters discuss several adjunctive approaches to antipsychotic drug treatment. These drugs are already given routinely in the community, sometimes without clear understanding of their indications, risks, and limitations. Having these spelled out in a concise way may prevent harm to the patients. Owen Wolkowitz et al. discuss the rationale and efficacy of adding certain benzodiazepines to traditional antipsychotic drug treatment. Although these authors are enthusiastic about the benzodiazepines, there are several caveats. There is a risk of tolerance development and addiction, and the condition may worsen on drug discontinuation. Seizures may occur on sudden discontinuation of high doses of alprazolam. This can be particularly serious in patients who are unreliable in their drug compliance. Wolkowitz et al. indicate that if patients do respond they will do so in the first 2 weeks, allowing the clinician to discontinue the drug early when it is ineffective to prevent unnecessary side effects. As long as we do not know how to identify the responders beforehand, the question of placebo response remains. Schulz et al. discuss lithium and carbamazepine as augmentation therapy. Fortunately, lithium has lost its bad name in schizophrenia treatment. Not so long ago a response to lithium was equated with a diagnosis of affective disorder. Since 1977 it has become clear that lithium has some antipsychotic effects by itself and even may affect negative symptoms. Although lithium supplements to neuroleptic treatment occasionally may lead to neurotoxicity, many patients are treated with it for better or worse. For that matter, antidepressants could have been discussed as well, and not only for the depressive component of schizophrenia.

Carbamazepine is the next drug of choice. It is popular among clinicians who interpret the patient's behavior as due to kindling or subthreshold seizure activity. Although the literature seems optimistic, the authors suggest that monitoring neuroleptic (and carbamazepine) blood levels may be necessary because carbamazepine may interfere with neuroleptic absorption. At present, patients with an epileptic focus or episodic violent outbursts may be the best candidates for this augmentation therapy. Carbamazepine does not seem to be effective as an antipsychotic agent by itself.

Jeffrey Berlant reviews the use of several different drugs that may decrease presynaptic dopamine synthesis or release. It is an interesting gallery of studies based on the hypotheses and clinical experience of the time. Inhibitors of synthesis include α -methyl-para-tyrosine, which may come back as a tool to study dopamine systems in man; reserpine, the first antipsychotic; γ -hydroxybutyrate; and presynaptic dopamine agonists. I feel that the book lacks here a discussion of the potential of enhancing dopamine activity in the frontal cortex, given the data of Bowers suggesting that dopamine may be decreased in neuroleptic nonresponders, and to counteract neuroleptic side effects that resemble negative symptoms. Occasionally, I have been asked to consult on patients who received amphetamine, L-dopa, or methylphenidate along with antipsychotic agents. Obviously, these drugs need to be given under careful supervision and by experienced clinicians because of potential exacerbation of psychotic symptoms, but the few studies addressing this question could have been discussed.

Of course, this book tells us about clozapine. John Kane et al. give a concise review of indications, response rates, and

side effects of this wonder drug. The question is whether it will be used, in view of the conservatism of psychiatrists. Surprisingly, in a recent study done in Europe about the need for new antipsychotic drugs, a majority of psychiatrists indicated that there were enough effective antipsychotics on the market today. However, as Kane et al. indicate, at least 30% of schizophrenic patients respond poorly and 10% may not respond at all to antipsychotic drugs. Clozapine is not a cure for schizophrenia, but it will decrease the symptoms of some of these patients. If clozapine can improve the mental status of an additional 10% of permanently psychotic patients, it will have served its purpose.

The book is well conceived and well written. The editors should be pleased. The pharmacological treatment of schizophrenia is becoming more hopeful as it is better understood. There is a feeling that we are at the threshold of knowing what works for our patients. There are now several new drugs similar to clozapine in different stages of development that will hit the market in the next 2 to 10 years. At that time the editors will be able to put out their next book or an updated version on the market, and it surely will be as needed as this one. Unfortunately, physicians have a hard time changing prescribing practices. A book like this may help those who are interested to improve their treatment practices. One hopes it will reach the next generation of practitioners. It should be compulsory reading for psychiatric residents, interested medical students, and other mental health workers who follow schizophrenic patients receiving medication.

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PSYCHOTHERAPY

Psychodynamic Psychiatry in Clinical Practice, by Glen O. Gabbard, M.D. Washington, D.C., American Psychiatric Press, 1990, 480 pp., \$49.95.

Great! Outstanding! Wonderful! Where has this type of book been the last 10 years? These were my thoughts as I read Glen Gabbard's new textbook on dynamic psychiatry. As Robert Wallerstein's introduction points out, we are in an era in psychiatric education that deemphasizes psychodynamic understanding, case formulation, and treatment planning. Dr. Gabbard's book convincingly puts the psychoanalytic dynamic view back into the "atheoretical" *DSM-III-R* classification of psychiatric disorders.

This book was written at the request of the editor-in-chief of the American Psychiatric Press. Dr. Gabbard is Director of the C.F. Menninger Hospital and a training and supervising analyst at the Topeka Institute for Psychoanalysis. He is a natural for this synthesis of psychiatry and psychoanalysis because his training and practice meld the inpatient and outpatient treatments of patients with different *DSM-III-R* diagnoses with a psychodynamic understanding of the clinical material. A major shortcoming of this book is that not all *DSM-III-R* categories are discussed. However, this marvelous

book does cover most of the relevant axis I and II categories. I hope Dr. Gabbard and his Menninger associates are planning a sequel that attempts to address each disorder in *DSM-IV*. As Dr. Gabbard notes, psychiatrists treating all mental illnesses, even the most biologically based, can find a sophisticated knowledge of transference, countertransference, and resistance extraordinarily helpful.

The book is organized into three sections: Basic Principles and Treatment Approaches, Dynamic Approaches to Axis I Disorders, and Dynamic Approaches to Axis II Disorders. The first section, which I found the best, elaborates the basic principles of dynamic psychiatry and presents overviews of the three main theoretical perspectives: ego psychology or classical Freudianism; object relations or the British (Kleinian) School; and self psychology or the Kohutian and interpersonal view. Dr. Gabbard's approach has a positive, accepting, and integrating style that makes one a believer in each theoretical view as he discusses them. The book is clear, concise, and straightforward, providing definitions and brief but clear explanations of the basic psychoanalytic concepts. Dr. Gabbard highlights the value of the psychiatrist's subjective experience. He defines psychodynamic psychiatry as "an approach to diagnosis and treatment characterized by a way of thinking about both patient and clinician that includes unconscious conflict, deficits and distortions of intrapsychic structures, and internal object relations."

Dr. Gabbard's discussions of the mental status examination, the dynamic interview, and the goals of psychodynamic therapy are excellent. He rightfully states that the clinician should let the patient lead the focus of treatment, but Dr. Gabbard's own orientation still focuses on the clinician's interpretations instead of the patient's psychic reality. My main complaint about the book is that it focuses too much on the object relations or Kleinian orientation. Marital therapy and hospital treatments are based exclusively on object relations views and the defenses of projective identification and splitting. Dr. Gabbard does not mention some of the current material from ego psychology, self psychology, and developmental psychology. I also think there is a lot more about group dynamics in general psychology and psychoanalysis than is represented in the work of Bion, Klein, and their followers, but Dr. Gabbard limits his discussions to these views.

This book is an admirable attempt by the author to integrate and be fair-handed about differing theoretical views, but he is unrealistic to think that clinicians can easily borrow views from one or another or can shift views. Much more often we see that the patient is fit into the therapist's theoretical view, and this dogmatic approach is most evident in the work of object relations theorists. Regarding the mechanism of change in expressive therapies, Dr. Gabbard correctly focuses on newer views of internalization and re-parenting from Hans Loewald's work, which highlights the therapy relationship as central to change in psychotherapy.

The specific sections on axis I and II are very good. Here Dr. Gabbard applies current psychodynamic thinking to schizophrenia, affective disorders, and many more, providing case examples for each. He carefully integrates and explains the value of dynamics in addition to biological components. There are also good sections on personality disorders in which Kernberg's and Kohut's differing views of borderline and narcissistic problems are contrasted.

This book is a must for all residents and psychodynamic clinicians.

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Supportive Therapy: A Psychodynamic Approach, by Lawrence H. Rockland. New York, Basic Books, 1989, 299 pp., \$24.95.

Have you had the experience of asking someone to explain what supportive therapy is only to receive a mind-numbing answer that fell somewhere between vagueness and being a nice person? Next time that happens, recommend this book. In fact, this highly readable, practical volume would be of benefit to more knowledgeable and experienced psychiatrists who would like to sharpen their skills in this area.

Rockland goes beyond defining supportive therapy. He describes what is supported, clarifies the differences between supportive therapy and exploratory therapy, discusses the situations in which supportive therapy should be considered, and examines the use of various combinations of supportive and exploratory therapy. He repeatedly gives clinical examples to illustrate the points he makes.

Holding true to the subtitle of the book, the author approaches supportive therapy from a psychodynamic perspective, focusing heavily on transference and resistance. However, throughout the book he is clear and consistent about the differences between exploratory and supportive approaches. An example is his repeated emphasis on confronting and dealing with negative transference and the complications of allowing it to grow in supportive treatment. The author's focus on the need for accurate assessment and diagnosis, his consistency of approach, and the clarity of his examples make this a very good book for residents and other developing psychotherapists.

Early in the volume Rockland develops his position that dynamically oriented supportive therapy is at least as challenging to conduct as exploratory therapy and often is more so. Supportive therapy requires a higher level of activity and therefore more decision making with the potential for more errors than is the case in exploratory therapy, where activities and interventions are rather structured. Additionally, in supportive therapy one is often working with patients endowed with substantial emotional limitations. In this regard, the author lays out rather clearly the complexities of the therapy. He discusses the stresses of working with patients who sometimes behave in an unpleasant fashion both in and out of treatment. Therapists who work in this less structured modality are also vulnerable to the hazards of overinvolvement. Rockland makes such a strong case for the value of dynamically oriented supportive therapy that one cannot help but wonder if it should be applied in more situations where exploratory therapy is used.

Wisely included is a chapter by Ann H. Applebaum, who draws parallels between the actions of parents that foster maturation and the activities of supportive therapists that increase the adaptive capacities of their patients. One can appreciate the extent that psychotherapy of any type rekindles that which is part of human biology and exists in relationships perceived as nurturant, although this idea is never formally addressed.

The section of the book dealing with technical aspects of therapy has excellent chapters on transference and countertransference as well as different aspects of treatment. Some wooden recounting of psychoanalytic literature crops up periodically, deadening, for example, the beginnings of the chapters on therapeutic alliance and working through. These may satisfy some need for homage but do little else.

The author's efforts to keep supportive therapy in a psychodynamic context pose a conflict not clearly addressed. How much psychoanalytic theory does one need to know to

do this kind of work? He correctly, I believe, advocates greater emphasis on teaching supportive therapy to residents. He believes that supportive work can be done by residents who receive sufficient instruction. However, his message is that *considerable* psychodynamic training is necessary. It may be that flexibility of approach and *enough* psychodynamic training are what is necessary. Lots of knowledge and little flexibility clearly will not work. The reverse leads to the horror of the "nice guy" approach to therapy, something Rockland would abhor.

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Cognitive Behaviour Therapy for Psychiatric Problems: A Practical Guide, edited by Keith Hawton, Paul M. Salkovskis, Joan Kirk, and David M. Clark. New York, Oxford University Press, 1989, 449 pp., \$60.00; \$24.95 (paper).

Although cognitive behavioral therapy traces its roots back to the experiments in classical conditioning of Pavlov, it is really only in the past decade and a half that it has expanded its focus sufficiently to be of great clinical value in the psychiatric setting. With its emerging attention to what humans think rather than just what they do, cognitive theory's marriage to behavior therapy has supplied us with a powerful new weapon in the psychotherapist's armamentarium. The assumption that we are what we think may have serious limitations as a general psychology, but this fundamental credo of cognitive theory has turned out to have tremendous value in the understanding and control of psychiatric symptoms. In *Cognitive Behaviour Therapy for Psychiatric Problems*, Hawton, Salkovskis, Kirk, and Clark have presented the psychiatric therapist with a remarkable summary of the current clinical practice of cognitive behavior therapy.

The book is fundamentally oriented to the practical application of cognitive behavioral therapy. Nonetheless, it begins with a concise chapter on the historical and theoretical underpinnings of the treatments presented. This is followed by a detailed chapter on the cognitive behavioral assessment of the psychiatric patient that is crisp and direct in its presentation of the need for and importance of careful assessment procedures. Like the rest of the book, it is basic and fundamental but well worth a careful reading by anyone interested in the evaluation and phenomenology of psychiatric symptoms. The rest of the book details the specific cognitive behavioral diagnostic assessment of and treatment strategy for a broad range of psychiatric symptoms and disorders.

Although this book is edited, it does not seem to suffer from the plethora of different writing styles and ideas often found in such volumes. Remarkably, it flows as if it were written by one person, and each chapter seems to build on information presented in previous ones or refers to ideas that are explained further in a later part of the text. This is very unusual for an edited book of such length and breadth and is a testimony to the care the editors took in editing and organizing the manuscripts. It may also be that the cohesiveness of the presentation derives in part from the similarity of the theoretical positions of the authors and the boundaries they chose to put around their subject. However, each chapter is organized similarly, ending with a section on alternative treatments and outcome studies, for example, so the uniform feeling of the book must be intentional. In any case, the book is wonderfully easy to read.

The different authors present the basic rationale for and description of the cognitive behavioral treatment of anxiety states, panic disorder, phobic disorders, obsessional disorders, depression, somatic problems (including headache, insomnia, and irritable bowel), eating disorders, sexual dysfunctions, and marital problems. Clearly, such an exhaustive list implies that the book does not attempt to explain all there is to know about each subject. On the other hand, enough material is presented to allow any practitioner not only to understand the essence of the treatment but to start an effective, informed cognitive behavioral treatment. This is definitely a "how to" book.

After pointing out their fundamental relationship to psychiatric symptoms, the book covers in sufficient detail the strategies for dealing with 1) negative automatic thoughts, 2) avoidance of feared ideas, objects, or situations, 3) neutralizing, and 4) dysfunctional beliefs. It then teaches the use of cognitive education, behavior exchange and experimentation, exposure, modeling, role playing, relaxation, imaging, distraction, problem solving, and a host of other useful techniques to control these thoughts and behaviors and thus change, reduce, or control the dysfunctional symptoms.

The book is strongest in its verbatim description of just what the therapist says to the patient and weakest when it minimizes the efficacy of alternative treatments, especially in its negative views of the adjunctive value of psychopharmacological therapy.

The great value of the text is that it is informative, useful, and practical. Although certainly not written for the active, advanced practitioner of cognitive therapy, it is for those of us who do not know enough about this subject. It is for the practicing analysts, general psychiatrists, and therapists of all persuasions who want (or maybe, need) to get a clearer notion of what cognitive therapy is all about. It is for the inquisitive student at any level of experience or training who once having read something interesting is prone to experiment with the information in the hope that trying something new can help patients overcome disabling psychiatric symptoms.

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Object Relations Group Psychotherapy: The Group as an Object, a Tool, and a Training Base, by Ramon C. Ganzarin, M.D. Madison, Conn., International Universities Press, 1989, 362 pp., \$40.00.

Since the mid-1970s, when it was given a most forceful articulation by the American psychoanalyst Otto Kernberg (1), object relations theory has gradually emerged as a major area in clinical psychiatry and psychology. Interest in and knowledge about the British School of object relations theory (represented by the work of Melanie Klein, Winnicott, Guntrip, and Fairbairn) has become widespread and shows no signs of abating. Object relations theory has broken out of the confines of psychoanalysis and entered into all areas of clinical endeavor. Numerous works have emerged that apply object relations theory to different clinical phenomena and activities, including theory (2), individual psychotherapy (3), marital and family therapy (4), the psychology of gender (5), and psychological testing (6). Object relations theory's nonabstract concept of "experience-near" has stimulated empirical research (7) and is interfacing with academic, social, cognitive,

and personality psychology. It would not be an overstatement to suggest that object relations theory is evolving into a dominant paradigm of clinical work in the United States.

A book applying object relations theory to group psychotherapy, therefore, should naturally fill an important niche in the evolving literature. Regrettably, *Object Relations Group Psychotherapy* only partially succeeds in the task. The book, for the most part a collection of previously published chapters with some introductions and a couple of chapters added, is authored by a veteran group therapist. The "group as a whole" outlook, a point of view expressed in the seminal writings of the Kleinian analyst Wilfred Bion, pervades the book's chapters. The Kleinian approach to group phenomena is rich and deep and has become institutionalized in "Tavistock" approaches to the study of groups (8).

The book is divided into sections dealing with theory, specific clinical issues, and the use of training groups. The theory and clinical sections are by far the most successful, acquainting the reader with the relatively obscure work of Bion (9) and the "group as whole" approach in contrast to interactional or interpersonal (10) approaches to group therapy. The final section of the book includes several potentially interesting pieces concerning the use of groups in psychiatric training, including some empirical research. Unfortunately, several of these chapters were originally published in the 1950s and 1960s, and the research methodologies are simplistic and outmoded by contemporary standards.

Given the emergence of object relations theory, fresh opportunities to reconceptualize various clinical phenomena and endeavors in terms of the new paradigm are presenting themselves. It appears that the book filling the group psychotherapy niche, focusing on theory, process, and technique, has yet to be written. Although *Object Relations Group Psychotherapy* has a few illuminating chapters, especially with respect to the presentation and application of Kleinian clinical concepts, its lack of comprehensiveness and its use of republished material detract from its value for group therapists and scholars wishing to broaden their horizons.

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EPIDEMIOLOGY

Epidemiology and the Prevention of Mental Disorders, edited by Brian Cooper and Tómas Helgason for the World Psychiatric Association. New York, Routledge, 1989, 360 pp., \$59.50.

This book is derived from papers presented at the ninth scientific symposium arranged by the World Psychiatric Association's Section on Epidemiology and Community Psychiatry, which took place in Reykjavik, Iceland, in September 1987. The authorship is international and varied. The subjects also vary widely, from alcohol screening instruments and risk factors for depression in octogenarians to world organization policy statements regarding prevention of mental disorders in developing countries. Certain issues appear repeatedly throughout the work, however, namely, suicide, affective illnesses, schizophrenia, and dementing illnesses.

The book is divided into six parts, and the introduction in the first part dictates the focus of the book. Dr. Cooper, one of the editors, authored this introduction, which enumerates the points to be investigated as follows: case finding and early detection, identifying and assessing risk factors, protecting the vulnerable individual, preventive action in health services, and promoting healthier public policies.

In the section on early detection William Eaton et al. focus on the definitions of incidence rates and the effects of different errors. They do an admirable job of taking well-known Epidemiologic Catchment Area data and explaining how application of traditional concepts of incidence and prevalence may be problematic and even misleading. Also in this section appears the application of screening techniques in communities, in this case for alcoholism, specifically systematic alcohol screening of general hospital admissions. These efforts appear to yield more accurate incidence rates than could be gleaned from a general population survey. It is important to note, however, that "the sensitivity of the screening instrument varied according to the hospital department in which it was used" (p. 9).

In the section on identifying and assessing risk factors, Norman Sartorius presents data from the International Pilot Study of Schizophrenia. These data clearly illustrate the distinction between factors that determine risk and those which influence prognosis. This chapter also points to the strong cultural influence on the natural history of mental illness and how its course may be modified by the mental health delivery system. For example, in developing countries the vast majority of schizophrenic individuals can be treated as outpatients, and their disease appears to have a milder course.

In the section on protecting the vulnerable individual, the editors emphasize the difficulties of trying to separate individuals at risk from the inherent risks of the environment on the individual. Ezra Susser et al. investigated the complicated interaction of homelessness and psychiatric illness in New York City, trying to unravel the causal links between illness and risk factors.

The section on preventive action focuses on reports of secondary and tertiary prevention, especially in European countries such as The Netherlands and Greece. The focus of much of this research has been on outpatients and on special efforts by the mental health system to avoid inpatient hospitalization. Finally, the section on promoting healthier public policies pays particular attention to improving mental health standards set down by political institutions. These policies have an impact,

especially when they target high-risk populations who suffer from mental illnesses that may have a preventable cause.

The editors have done an excellent job of demonstrating the power inherent in the epidemiology of mental disorders. They challenge the reader to examine mental illness as a dynamic process that can be conceptualized and, with careful planning and cooperation, may even in some instances be preventable. The importance of prevention of mental disorders and research on such prevention has become the target of a recent APA task force (1). Interest in this field, however, has been lacking. Because of this paucity of interest, this text seems more appropriate for researchers in psychiatry, epidemiology, and preventive medicine than for the psychiatrist in general practice.

Finally, a couple of problems deserve mention. First, because of its many authors the book does not flow evenly throughout, even though it does have several very strong chapters. Second, the rather steep price does not lend itself to wide readership by general psychiatrists. Nonetheless, this well-structured text is needed and warmly welcomed.

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H. MIKEL THOMAS, M.D.
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Data Quality in Longitudinal Research, edited by David Magnusson and Lars R. Bergman. New York, Cambridge University Press, 1990, 285 pp., \$54.50.

This work presents a series of thoughtful discussions about the longitudinal study of development. The chapters represent the concerns of a variety of disciplines (e.g., psychiatry, psychology, sociology, and epidemiology). Since the authors are multinational, the effort draws on the experience of a number of researchers involved in a range of national longitudinal studies. The effect of this diversity of fields and national traditions with a common focus on quality of data in longitudinal study is a collection of chapters that are intrinsically interesting. The overlap of issues across traditions and subjects allows the chapters to fit together very well and illustrates how solutions to common issues are reached via different paths. The

chapters are well written; however, none is particularly light reading.

An introductory chapter reviews, among other general issues, the concepts of reliability, validity, hypothetical constructs (in contrast to measurable empirical constructs), and the effects of attrition. The authors discuss these in the context of the longitudinal study, using a gentle blend of classical test theory and structural modeling. The chapters that follow are arranged into three sections.

Part one consists of issues in longitudinal studies in psychiatry, epidemiology, pediatrics, and the study of alcoholism. This section serves as a showcase for the theoretical developments that longitudinal data can provide by examining issues and focusing on problems and their solutions. A concluding chapter deals with the use of retrospective reports in social science and medical fields of study.

Part two includes two chapters about attrition over the course of a longitudinal study and its potential effects on data quality and the inferences that researchers can make. The authors again focus on problems and solutions by emphasizing methods of reducing attrition and lessening its impact on conclusions.

Part three, Design, Methods and Data Quality, addresses a conglomeration of issues rather than a specific topic. Chapters deal with the archiving of data, the use of qualitative case study material, patterns of stability and stability of patterns, and the inclusion of intergenerational factors. Again, many of these chapters are showcases of longitudinal studies, approaches, and theoretical developments (e.g., separating age, period, cohort, and historical events).

This book as a whole is quite good. Admittedly, I do not know that I would have freely read through all of the chapters because it did get dense at times. Little or no formal training in mathematical statistics is required, and the level of the book is more conceptual, focused on planning. The relevance of the topic of current discussion was almost always either obvious or explained, except perhaps the chapter "N's, Times and Number of Variables in Longitudinal Research," which, by the way, did not tell you what your sample size should be—as the title might suggest. That the phrase "quality data" means a variety of things is accurately represented with force by the variety of topics. I also finished the book even further impressed by how rich the information is that can be obtained from a well-designed longitudinal study.

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Reprints of Book Forum reviews are not available.

Letters to the Editor

Fluoxetine and Preoccupation With Suicide

SIR: In a reply to letters to the Editor (1), Martin H. Teicher, M.D., Ph.D., and associates mentioned that Dr. Barbara Geller had discontinued an open study of fluoxetine in adolescents because of side effects. This is a misstatement. We have never performed any protocol or any investigation on fluoxetine in adolescents. We have never presented this type of material at a meeting. Dr. Geller did mention to Dr. Teicher, in an informal discussion, that we had some routine clinical experience with fluoxetine. Although we do not believe that the misstatement should in any way alter the important emphasis that Dr. Teicher and associates have given to improving patient care by carefully monitoring possible side effects of new medications, we do feel that this correction needs to be published.

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HAZEL E. WATTS, B.S.N.
BARBARA GELLER, M.D.
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SIR: The concept of antidepressant-induced suicidal ideation put forward by Martin H. Teicher, M.D., Ph.D., and associates (1) on the basis of their finding that fluoxetine can cause suicidal ideation, introduces into psychiatry a new and dangerous precedent. What these authors are saying unrealistically elevates the power of psychopharmacology to a mythical height where psychotropic drugs not only tranquilize anxious or depressed emotions but also have a capacity, in susceptible persons, to induce a specific thought process, such as suicidal ideation. Why stop at a concept of antidepressant-induced suicidal ideation? The hypothesis can as easily be extended to psychotropic-induced homicidal thoughts (as was done by one patient, reported in the media, who claimed that triazolam induced her to commit murder), thoughts of property destruction, incestuous thoughts, thoughts of divorce, and so forth.

Psychotropic medication may be the instrument of suicide but not the cause. Liability for suicide can only be attributed on the basis of failure to recognize reasonable predictors, not on the basis of a speculative theory that an antidepressant medication may act paradoxically and cause suicide instead of preventing it. If, as Dr. Teicher and associates recommend, patients taking fluoxetine should be informed of the possibility of medication-induced suicide, then every single drug in the practice of medicine—psychotropic and nonpsychotropic alike, such as diuretics, antihypertensives, and steroids that may cause depression—would require a similar ominous warning to patients. This would make the practice of medicine burdensomely restrictive, but of course it would be very ap-

pealing to plaintiff attorneys who frivolously and erroneously cite cause-effect relationships between time-associated but unrelated phenomena.

The historical course of fluoxetine may follow the fate of other psychotropic drugs found to be effective and widely prescribed. Two examples are methaqualone and diazepam. Unfortunately, when a psychotropic drug is prescribed for an individual with a personality disorder, and subsequently some behavioral pathology transpires, it is so easy for the patient to be absolved of personal responsibility and to link the behavioral problem, whether this is suicide or something else, to the prescribed drug.

It is small wonder that nonprescribing psychologists are winning more and more of the mental health care turf, since some psychiatrists, whatever else they are expert in, seek to be proficient in self-destructive indictment of many of our useful psychopharmacological tools.

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SIR: In an article by Martin H. Teicher, M.D., Ph.D., and associates (1), a relation between fluoxetine and suicidal ideation was reported in six patients. Although controlled clinical trials with the drug have not led to such findings (2-4), these authors' cases support the need for further research.

In my opinion, there may be a predisposition for suicidal ideation and behavior in patients taking fluoxetine who have previously been treated with monoamine oxidase inhibitors (MAOIs). In the cases of Dr. Teicher and associates' patients who became suicidal when taking fluoxetine, all six patients had prior experience with MAOIs. For three of these patients (cases 2, 3, and 5), a washout period of 2 weeks' duration was specified before fluoxetine was administered. Unfortunately, we have no information about when MAOIs were discontinued in the other patients.

A second issue is that of drug-drug interaction when neuroleptics are prescribed with fluoxetine. In Dr. Teicher and associates' article, there were definitely two patients (cases 3 and 6) who were taking neuroleptics, some of which were prescribed in high doses, before fluoxetine was added. In addition, the patient in case 1 was being treated with amoxapine, an antidepressant with neuroleptic activity. Despite a 4-week washout of amoxapine before fluoxetine, the possibility that there were some active metabolites still present when fluoxetine was added cannot be ruled out, and this may have caused akathisia or akinesia. In fact, in three of the six patients, this kind of interaction cannot be ruled out. If we look at case 1, the patient is described as feeling like "jumping out of her skin," with no signs of motor restlessness, which is compatible

with subjective akathisia. In case 3, where fluoxetine was added to high doses of perphenazine (20 mg), we see a worsening of akathisia until perphenazine was decreased. However, we also see that akathisia persisted, as shown by poor concentration and an increase of binge eating. In case 6 there is evidence that by week 7 of the fluoxetine regimen the patient had become restless and agitated. I feel that fluoxetine taken with neuroleptics could increase suicidal ideation in patients who become akathisia or akinesic by exacerbating the parkinsonism induced by neuroleptic drugs. This could possibly be caused by an inhibition of the metabolism of neuroleptics or of fluoxetine or through an indirect effect on the dopamine system (5).

If a study were specifically designed to test hypotheses regarding the relation between previous MAOI and neuroleptic treatment and fluoxetine in the emergence of suicidal ideation, I would suggest the measurement of 5-hydroxyindoleacetic acid (5-HIAA), in those patients who have previously been treated with MAOIs in particular, to see whether a low 5-HIAA value predisposes patients to suicidal ideation whenever fluoxetine is given.

At the present time, I would suggest that fluoxetine be formally contraindicated for patients who are taking neuroleptics and, in the case of patients who have previously been receiving MAOIs or neuroleptics, the withdrawal washout period be increased to 5 weeks before fluoxetine is initiated.

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SIR: In their article (1), Dr. Teicher and associates described six cases of intense suicidal preoccupation that occurred during fluoxetine treatment. The authors' initial surprise that this response was evoked by a potent and selective serotonergic uptake inhibitor arose from the common assumption that increasing serotonergic activity should counter suicidal tendencies (2).

In reviewing their cases, I note that a common feature was the emergence of either restlessness or lethargy. Perhaps this is due to fluoxetine's ability to affect the extrapyramidal motor system, with either a *de novo* induction or a worsening of extrapyramidal symptoms (two patients were already receiving neuroleptics). Lipinski et al. (3) previously reported that fluoxetine can induce akathisia and hypothesized that this is due, at least in part, to enhanced serotonergic neurotransmission. Meltzer (4) has hypothesized that the relative lack of extrapyramidal side effects of the atypical antipsychotic clozapine may be due to its high degree of serotonin antagonism, again suggesting that serotonin activity affects nigrostriatal

function. Preclinical studies also demonstrate that serotonin activity affects neuroleptic-induced catalepsy, the animal equivalent of extrapyramidal symptoms, in rats (5).

Perhaps in an already severely depressed patient, the appearance of unexpected motor side effects, experienced as either increased "restlessness" or increased "lethargy," could be viewed with alarm and give rise to suicidal thinking.

The existence of potent serotonergic agents increases our pharmacotherapeutic armamentarium but requires us to increase our understanding of the multiple systems affected by these agents. Dr. Teicher and colleagues are to be praised, not castigated, for alerting us to these potential complexities.

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SIR: In a reply to a letter to the Editor (1), Dr. Teicher and associates wondered about the development of suicidal ideation in patients treated with fluoxetine for disorders other than depression. Our experience with 56 women treated with fluoxetine over the last 2 years for late luteal phase dysphoric disorder (LLPDD) seems pertinent to this matter.

The 56 patients ranged in age from 24 to 45 years (the average age was 36 years). Most were married and employed. They all met the *DSM-III-R* criteria for LLPDD. None had a concomitant psychiatric disorder as determined by the Schedule for Affective Disorders and Schizophrenia interview (2). None was taking other psychotropic medications. The mean length of follow-up has been 10.8 months (range=1-18 months). Each woman was assessed monthly for the first 4 months of treatment and subsequently at 3-month intervals with a clinician checklist that included a question about suicidal ideation. The women were treated with either 20 mg (N=42) or 40 mg (N=14) of fluoxetine daily. Fifty-two women showed substantial relief of LLPDD symptoms. Treatment-emergent side effects have included insomnia, decreased libido, and urinary frequency. None of our subjects has developed suicidal ideation.

Our findings suggest that while some depressed patients may develop intense suicidal preoccupation while taking fluoxetine (3), fluoxetine itself may not be sufficient to produce this symptom. There may be a small subgroup of patients who are vulnerable to the development of suicidal ideation during treatment with fluoxetine, as well as other antidepressants (4). It is worthwhile for all clinicians to contribute to the body of knowledge regarding patients who may have a propensity for developing suicidal ideation while taking fluoxetine, not only so that they may be identified but also so that

other patients who may benefit from this treatment will not be denied it unnecessarily.

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SIR: When one of my patients killed himself years ago, the lawyers blamed not imipramine but me. I regret that fluoxetine was not available then (1).

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Dr. Teicher and Associates Reply

SIR: We thank the Editor of the *Journal* for publishing the article on our series of cases and our colleagues for sharing case material and providing thoughtful comments. When we submitted our report for publication, we had no conception of the type of response it would provoke. We hope that the intense media reaction has had some positive value in encouraging more open communication about the treatment of depression, and we trust that we have stimulated our colleagues to examine more critically the relative risks and benefits of treatment.

First, we apologize to Dr. Barbara Geller and her associates for Dr. Teicher's misstatement. When she spoke with him at a National Institute of Mental Health workshop on adolescent depression, and she described her clinical experience in observing the emergence of severe suicidal or homicidal ideation in some adolescents receiving fluoxetine, he thought it was in the context of an open trial. He stands corrected. We hope, however, that Dr. Geller and colleagues will choose to publish a report of their clinical experience in this matter, as they have enormous expertise in the pharmacological treatment of adolescent depression. Fortunately, some important data on the emergence of suicidal ideation in nondepressed adolescents treated with fluoxetine (for obsessive-compulsive symptoms) have been reported by King et al. (1).

Second, we were surprised by the letter from Dr. Pearlman.

We suspect that he missed an important point by suggesting that psychotropic drugs only "tranquelize anxious or depressed emotions" and do not affect thought processes. He clearly failed to consider the action of antipsychotic and antiobsessive drugs. These agents dramatically affect thought processes by blocking or attenuating psychotic and obsessive ideation. One of the pivotal pieces of information leading to the dopamine hypothesis of schizophrenia was the observation that chronic stimulant abuse often creates a state of intense paranoia resembling paranoid schizophrenia (2). Similar effects can also occur during treatment with dopamine-mimetics in Parkinson's disease (3) and in the treatment of pituitary tumors (4). Innumerable other agents, including many used in general medicine, can induce psychosis and have been reported to produce paranoia, grandiosity, religious delusions, Capgras' phenomenon, delusional belief that one has died, parasitosis, and delusional belief in ability to fly. Indeed, MEDLINE lists 2,329 references on drug-induced psychoses. We hope that psychiatrists have a clear appreciation of the potential of medications to induce prominent disturbances in thought processes, perception, and reality testing and that they recognize that this is an important component in the evaluation of patients with thought disorders. Unfortunately, we know less about the neurobiology of obsessional thinking, but recent studies have provided important clues about the anatomy, pathophysiology, and neuropharmacology of obsessions (5). Since drug regimens that attenuate obsessive ideation have been identified, it is rather likely that regimens that induce obsessions will receive increasing recognition.

Our basic hypothesis (elaborated below) is that fluoxetine does not necessarily create specific thoughts in susceptible individuals. Even healthy individuals may have fleeting inconsequential thoughts of suicide or homicide. The serotonin system may play a pivotal role in enabling us immediately to dismiss these thoughts from consciousness and to prevent us from acting on our aggressive impulses (5). Drug-induced imbalances may cause patients to be unable to dismiss these thoughts, leading to ego-alien obsessions; or drugs may compromise the behavioral inhibitory system, leading patients to act impulsively on these thoughts in a manner that is clearly out of character. We hope that Dr. Pearlman is aware that there is an extensive literature (e.g., 6) on benzodiazepine-induced rage reactions and disinhibition, which can lead to violence and destruction of property.

Overall, there is emerging evidence that some medications can precipitate, exacerbate, or rekindle suicidal ideation. Certainly, patients who are prescribed medications that can induce depression should be informed about this possibility, and warning signs and risks should be discussed—including the risk of suicide. This does not make the practice of medicine overly burdensome or restrictive. Rather, it forewarns patients, so that they can more readily recognize that these are side effects, and should empower them to seek appropriate help rather than suffer needlessly or act on their feelings. Perhaps Dr. Pearlman would benefit from reading William Styron's book *Darkness Visible* (7), in which he states his belief that high-dose triazolam triggered his obsessive suicidal ideation. Honestly informing our patients about the power and perils of psychotropic medications will not drive them into the arms of psychologists, who clearly covet our prescribing privileges. We are far more likely to alienate patients by failing to warn them about important adverse effects or, worse yet, by refusing to believe their reports. We may bring more patients into treatment by claiming that we have miracle drugs free of serious adverse effects, but such claims, when untrue, will undoubtedly provoke a vociferous backlash.

Dr. Chouinard and Dr. Opler raise questions about the association between the emergence of suicidal ideation and the induction or exacerbation of akathisia or akinesia. Clearly, fluoxetine can induce akathisia (8), and this effect may lead to substantial behavioral toxicity. We do not, however, believe that there is a direct causal relation between this change in motor tension and the emergence of suicidal thoughts or impulses. Rather, we suspect that these symptoms reflect similar forms of neurochemical imbalance in distinct but related systems. Thus, we suspect that fluoxetine-induced motor effects may be related to the important modulatory effect which serotonin exerts on dopamine (9, 10) and that these interactions may occur principally in the striatal system, which controls the induction and initiation of motor activity. Excessive serotonergic inhibition may antagonize motor activity (9), and loss of serotonergic inhibition, through receptor desensitization (11) or attenuated serotonin release (12), may produce excessive motor activity (9). We suspect that serotonergic effects occurring in the ventral striatum and prefrontal cortex may produce disturbances in thought processing and impulse control. Excessive serotonergic neurotransmission in these regions is hypothesized to be the crucial underlying state in obsessive-compulsive disorder (5). As suggested by Papp and Gorman (13), producing this neurochemical state in some susceptible depressed patients may cause them to have vehemently obsessive suicidal thoughts that would otherwise pass through consciousness as fleeting thoughts of no importance. As we observed in many of our patients, they had endless obsessions but were relatively inhibited in acting on these obsessions, which is consistent with an overactive behavioral inhibitory system (14). On the other hand, a loss of serotonergic neurotransmission in these regions might seriously compromise patients' behavioral inhibitory systems, leading them to act impulsively on these thoughts and to be basically unable to control their actions (14). Thus, an obsessive but inhibited suicidal state may be seen in conjunction with symptoms of akinesia or excessive fatigue or abulia, and all may stem from excessive serotonergic activity in different projection pathways. Similarly, an impulsive, disinhibited, self-destructive or violent state may coexist with intense akathisia or restlessness, and both may be a consequence of reduced serotonergic neurotransmission in related projection pathways.

We believe that Dr. Chouinard pushes too hard to blame these reactions on an interaction between fluoxetine and neuroleptic drugs. First, he is mistaken in stating that some of our patients received high doses of neuroleptics. Only two patients received neuroleptics concomitantly with fluoxetine. The patient in case 2 received perphenazine, 12–20 mg/day, and the patient in case 6 received haloperidol, 4 mg/day. On the basis of approximate tables of potency (15), both dosage regimens were only about 200 chlorpromazine equivalents, and therefore they both represent low-dose treatments (16). Similarly, his point that the patient in case 1 may have experienced some neuroleptic effects from amoxapine after a 4-week washout period is unlikely, as she had experienced no significant neuroleptic-like effects even during treatment. Furthermore, we have found the strongly antiserotonergic neuroleptic chlorprothixene to be effective in attenuating some of the distress, agitation, and intensive suicidal preoccupation associated with fluoxetine treatment in a few cases. In short, fluoxetine in and of itself is capable of producing both akathisia and akinesia. Neuroleptics may exacerbate these effects, but we suspect that they were neither necessary nor sufficient components of these reactions. Similarly, we do not believe that previous treatment with MAOIs is a necessary precondition. It

appears that in the four additional reported cases in adults (17–19) and four additional cases in adolescents (1), the patients had probably not received prior MAOI therapy.

We thank Dr. Stone and associates for sharing their experience in using fluoxetine for the treatment of LLPDD. We agree wholeheartedly that it is important for clinicians to share their experience so that we can more readily identify patients who are likely to benefit and those who may be more at risk for developing significant adverse responses. Current theories on the pathophysiology of LLPDD often identify a sharp premenstrual decline in plasma serotonin levels (20, 21) or platelet serotonin uptake (21–23), consistent with a hypothesis of abnormal cyclical fluctuations in serotonergic activity (24). It is possible that low doses of fluoxetine effectively stabilize this system, which otherwise would show abnormal hysteresis, and thus this may be a very effective and appropriate treatment.

Finally, we are at a loss as to how to respond adequately to Dr. Balon's succinct comment. Perhaps this is an appropriate place to indicate that other drugs, possibly through different mechanisms, may either induce suicidal thoughts or facilitate suicide attempts. The most interesting data on this point, which we have only recently become aware of, are from a 1-year double-blind, prospective, placebo-controlled trial of maprotiline in patients with major depression (25). The investigators found that suicide attempts occurred only in patients taking active medication (nine of 521), not in placebo-treated patients (none of 212), although maprotiline was clearly effective in reducing depressive symptoms. Similarly, we should remind readers of the observation of Soloff et al. (26) that nearly half of their borderline personality disorder patients who received amitriptyline experienced worsening of depression, behavioral dyscontrol, or enhanced suicidal preoccupation. In case reports, emergence of suicidal ideation has also been linked to treatment with desipramine (27), diazepam (28, 29), and doxepin (30).

We hope that our article has brought this issue into greater focus, so that we can learn how to use these important medications as safely and as effectively as possible.

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Appearance of Obsessive-Compulsive Symptoms in Depressed Patients Treated With Fluoxetine

SIR: Recent uncontrolled studies of fluoxetine suggest that it is useful in the treatment of obsessive-compulsive disorder (1-4). We, however, observed the onset of obsessive-compulsive

symptoms in three patients who presented with depression and were treated with fluoxetine. We are reporting these cases to determine whether others have observed these effects in treating patients with fluoxetine.

The patients had certain characteristics in common. None had a previous history of obsessive-compulsive disorder, none had a family history of obsessive-compulsive disorder, Tourette's syndrome, or tics, and they all developed obsessive-compulsive symptoms within 4-5 weeks after initiation of treatment with fluoxetine. Each patient presented with depressed mood, poor appetite, thoughts of death, and poor concentration. Each was treated with individual psychotherapy and started on a regimen of fluoxetine, 20 mg/day.

Ms. A, a 21-year-old woman, presented also with psychomotor retardation, withdrawn behavior, and insomnia. After 5 weeks of treatment with fluoxetine and psychotherapy, she began reporting that she was preoccupied with counting letters in books and advertising posters. The depressive features were not yet subsiding, so her dose of fluoxetine was increased to 20 mg b.i.d. With this, the obsessive-compulsive symptoms increased, and the patient stopped taking the medication and dropped out of treatment for 6 months. She resumed treatment, reporting that the obsessive-compulsive symptoms had stopped 2 weeks after she discontinued medication. Subsequent treatment with doxepin hydrochloride and individual psychotherapy has resulted in improvement in her functioning and self-esteem.

Ms. B, 28 years old, developed depressive symptoms with insomnia and guilt feelings and could not go back to work after a spontaneous abortion. Four weeks after starting fluoxetine and individual psychotherapy, she began to complain that she felt compelled to count the people and remember all the details of television programs and to count all the people in the subway car. Her medication was discontinued, and after 4 weeks of supportive individual psychotherapy and couples therapy, the obsessive-compulsive and depressive symptoms subsided and she went back to her job.

Ms. C, a 54-year-old woman, had migraine headaches in addition to the depressive symptoms common to this group. A neurological work-up revealed no specific finding. She continued to take butalbital and started fluoxetine. After 5 weeks, she reported compulsively counting doors and windows of buildings and houses. She refused to go out of the house because people would observe her compulsion and say that she was crazy. Medication was discontinued after 9 weeks of treatment, and the obsessive-compulsive symptoms abated. A few weeks later, treatment with doxepin hydrochloride was begun, and her depression eventually subsided.

While the two younger women were not past the age of vulnerability for developing obsessive-compulsive disorder, these findings suggest that the effects of fluoxetine on obsessive-compulsive symptoms may not be straightforward and that there may be some complexities of serotonin and receptor functioning that need to be taken into account. A study of the serotonin agonist metachlorophenylpiperazine (mCCP) produced a transient, marked increase in symptoms in patients with obsessive-compulsive disorder (5). The authors who reported this finding hypothesized that long-term treatment with mCPP, fluoxetine, and other agents that are believed to increase serotonergic functioning indirectly may lead to an

adaptive down-regulation of postsynaptic serotonin receptors.

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Extrapyramidal Symptoms Upon Discontinuation of Fluoxetine

SIR: We wish to report the following case.

Mr. A, a 32-year-old white man, came to the hospital emergency room with an acute dystonic reaction involving the extensors of the neck, back, and upper extremities and torticollis. His past medical history included major depression of approximately 6 months' duration. He had been taking fluoxetine during the past 6 months, and the treatment had been discontinued 2 days before he came to the emergency room. He reported that on the day before he presented there was some stiffness in his neck. He went to a cocktail party the evening before and awoke in the morning with painful extensor muscle spasms and protruding tongue movements. The patient denied use of any recreational drugs or any prescription medications. Physical examination revealed a pulse of 100 bpm, a temperature of 99° F, and blood pressure of 180/100 mm Hg; he was diffusely diaphoretic and tremulous, with protuberant tongue movements that were suppressible while he was speaking. Motor tone in the extremities was increased without cogwheeling. Laboratory data were within normal limits, and the toxicology screen was negative. The patient was treated with 50 mg i.m. of diphenhydramine, and complete resolution of symptoms occurred over the following 45 minutes.

The development of extrapyramidal symptoms has been reported in patients while they were taking fluoxetine. However, this report involves a patient taking no other medications who developed symptoms only upon discontinuation of fluoxetine therapy. Meltzer et al. (1) reported dystonic reactions and parkinsonian rigidity in a patient taking fluoxetine. Tate (2) reported severe, intractable extrapyramidal symptoms in a patient taking both haloperidol and fluoxetine. In another report (3), five patients with preexisting parkinsonian movements showed worsened bradykinesia and rigidity after the introduction of fluoxetine. In two cases fluoxetine was the only prescribed agent. There has also been a report (4) of a patient

with cerebral palsy who developed severe, generalized muscular stiffness over 8 days while taking fluoxetine, 20 mg/day (on 5 of these days the patient was also taking haloperidol, 1 mg).

Lipinski et al. (5) reported patients who developed a fluoxetine-induced akathisia indistinguishable from neuroleptic-induced akathisia. The authors suggested that the akathisia may have been caused by serotonin-mediated inhibition of dopamine neurotransmission. Kim et al. (manuscript submitted for publication, 1991) noted the antidopaminergic effect of another serotonin reuptake inhibitor, clomipramine; the agent exhibited neuroleptic-like effects in patients with obsessive-compulsive disorder.

It appears from reports in the literature that fluoxetine, when used alone or in combination with neuroleptics, may exacerbate or cause extrapyramidal symptoms. The persistence of symptoms in some reports is consistent with the half-life of fluoxetine's active demethylated metabolite norfluoxetine, which is 7-15 days. Unlike case reports in the literature in which symptoms of extrapyramidal movement disorders developed with the addition of fluoxetine to neuroleptic therapy or with the use of fluoxetine therapy alone, our patient experienced no symptoms of extrapyramidal movement disorder while receiving active therapy but developed symptoms only upon discontinuation of therapy. We have been unable to find similar reports in the literature.

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Mania and Fluvoxamine

SIR: Fluvoxamine, an antidepressant that acts by inhibiting the reuptake of serotonin (1), has only recently become available in Italy. During treatment of patients with bipolar depression with a combination of fluvoxamine and lithium, we observed three cases of mania.

Mr. A, a 26 year-old man, had suffered from recurrent depression since he was 19. After a 3-year period of treatment with amitriptyline, he experienced a hypomanic episode of short duration. He had been affected by a major depressive episode for 9 months when he was observed in our outpatient department. He had received amitriptyline, sulpiride, intravenous imipramine, rubidium, and lithium salts with no benefit. Thus, therapy with 200 mg/day p.o. of fluvoxamine was initiated without discontinuing lithium

(serum level=0.50 meq/liter). After 5 weeks of treatment, Mr. A suddenly became manic and needed hospitalization. Treatment with fluvoxamine was interrupted, and neuroleptic medication was started. After 1 week the patient improved, but within a month his depression reappeared.

Mr. B was a 36-year-old man with a 6-year history of major depressive episodes. Previous episodes had been treated with tricyclic antidepressants. When he came to us, the patient complained of a major depressive episode of 2 months' duration that had been treated with classic antidepressants without benefit. Therapy with fluvoxamine, 100 mg/day p.o., and lithium (serum level=0.55 meq/liter) was prescribed. After 4 weeks of treatment, his mood improved, but he began to show mania with disinhibition, logorrhea, motor hyperactivity, and decreased need for sleep. Fluvoxamine was discontinued; the patient continued to take lithium and gradually became euthymic.

Ms. C was a 61-year-old woman who had been suffering from bipolar depression for almost 20 years. She had had only one hypomanic episode, with no temporal relation to depression or antidepressant treatments. She had been taking lithium for about 15 years and had responded well to it, and it was decided that lithium would be gradually reduced and suspended. Four months after discontinuation of the lithium, Ms. C manifested a depressive episode and was treated with 100 mg/day p.o. of fluvoxamine. After 20 days of treatment her condition improved, and lithium was added to the antidepressant therapy (serum level=0.60 meq/liter). However, 10 days later Ms. C became manic. Fluvoxamine was discontinued, and the dose of lithium was increased to achieve a higher level (0.86 meq/liter). Four months after discontinuation of fluvoxamine, she remained euthymic on the lithium regimen.

Our observations confirm the efficacy of fluvoxamine in the treatment of depression but suggest that this drug can induce mania in some patients when it is given at normal doses. This possibility has been well described for tricyclic antidepressants (2), and some reports also concern fluoxetine (3). In our cases, the occurrence of mania would seem to be related to fluvoxamine. In fact, our patients had previously responded poorly to classic antidepressants; only Mr. A once showed very mild euphoria of short duration despite extensive antidepressant treatment. Our findings suggest that the combination with lithium at low levels does not prevent mania but might enhance fluvoxamine activity. Moreover, caution is required during treatment of bipolar depression with fluvoxamine even when it is combined with lithium.

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Triazolam Accumulation in the Elderly After Prolonged Use

SIR: It has been generally believed that triazolam does not accumulate when used chronically because it has a very short half-life. This belief was based on the study of relatively young subjects or short periods of administration. However, triazolam has a greater propensity to produce daytime anxiety and cognitive impairment in the elderly after prolonged use (1). In this study, we examined whether triazolam accumulates in the elderly after chronic administration.

The subjects were 39 patients (13 male) with insomnia whose ages were 22-85 years (mean±SD=54±22 years). Informed consent was obtained from each patient. Nine were inpatients, and the rest were outpatients whose compliance with the drug regimen was assured by the family members living with them. None of them took other benzodiazepines, barbiturates, or cimetidine. All of the patients had normal creatinine levels and normal values on liver function tests (S-AST, S-ALT, alkaline phosphatase, and bilirubin). The dose of triazolam was adjusted to be optimal for controlling insomnia. Blood samples were collected after 4 weeks of daily intake. The average interval between blood collection and the last triazolam intake was 11 hours.

Triazolam has potent affinity for the benzodiazepine receptor and can have pharmacological effects at a very low level, which is difficult to detect by the conventional chemical method. In addition, triazolam is transformed into a potent active metabolite, α -hydroxytriazolam. Therefore, we decided to measure triazolam in serum by radioreceptor assay (2), which indicates total benzodiazepine receptor binding activity.

In all of the patients, insomnia was improved. The mean±SD daily dose of triazolam was 7.2±3.3 ng/kg. For 19 patients (seven inpatients), benzodiazepine receptor binding activity was detected in the serum collected in the morning. Fourteen of these patients were female. The average age of the patients in whom this activity was detected (65±17 years) was significantly higher than that of the rest of the patients (43±20 years) ($t=3.59$, $df=37$, $p<0.002$). However, the average daily dose was not significantly different in the two groups (7.4±3.1 ng/kg versus 7.0±3.7 ng/kg; $t=0.42$, $df=37$, $p>0.50$). Of the 18 patients who were 60 years old or older, serum benzodiazepine receptor binding activity (range=25-840 ng/ml of diazepam equivalents) was detected in 13 patients. On the contrary, of the 21 patients who were younger than 60 years, serum benzodiazepine receptor binding activity (range=30-170 ng/ml of diazepam equivalents) was detected in only five patients. Thus, triazolam was detected more frequently in the elderly ($\chi^2=11.35$, $df=1$, $p<0.001$). The usual therapeutic level of diazepam for anxiety has been reported to be 300-400 ng/ml (3). The highest benzodiazepine receptor binding activity observed in this study was 840 ng/ml of diazepam equivalents, which may be a toxic level.

In conclusion, in contrast to the general belief, triazolam is likely to accumulate in the elderly after chronic use. Our results were in accordance with a report that triazolam undergoes oxidation and that most of the benzodiazepines that undergo oxidation have age-related prolongation of half-life (4). Some patients had potentially toxic levels of benzodiazepine receptor binding activity, which might be associated with the adverse effects of triazolam. Sensitivity of the CNS to benzodiazepines increases in the elderly (5). Thus, both pharmacokinetic and pharmacodynamic changes are disadvantageous to the elderly, which may explain why adverse effects of triazolam are frequently seen in this group.

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Lorazepam in the Treatment of Catatonia

SIR: We write to describe an unusual response to lorazepam and *d*-amphetamine sulfate in a mute 31-year-old patient with catatonic schizophrenia.

Mr. A was found in a fetal position in his parents' home and was hospitalized. Available information indicated that he had become withdrawn and minimally communicative about 8 years earlier. He would come to his parents' kitchen for nourishment but otherwise remained withdrawn and seclusive. For several months before his hospitalization, Mr. A had periodically become quite agitated. He threw objects around the kitchen on several occasions but avoided hurting anyone. He had not left the house for a year and had refused to bathe or change his clothes for a month prior to this hospitalization (his first).

Mr. A's history included a motorcycle accident 10 years prior to admission. Although he incurred some trauma to his head, he did not lose consciousness and did not seek medical attention.

Mr. A's mother suffered from depression and angry outbursts. His brother may be an alcoholic. His maternal grandmother was "bizarre." Mr. A performed poorly in school, where he received Ds and Cs. He had a history of possible illicit drug use, including LSD, but none in recent years.

The initial physical examination was compromised because of Mr. A's passive resistance to being examined. His mental state examination was notable for his lack of cooperation and persistent downward gaze. He remained mute, rocked to and fro, shook his legs, and held his head with his hand. A CT scan of the head, a magnetic resonance imaging scan, and an EEG were unremarkable.

He failed to respond to sequential treatment with ECT (20 treatments); imipramine, up to 150 mg/day; fluoxetine, up to 40 mg/day (imipramine and fluoxetine were each given over several weeks, not concurrently); and haloperidol, up to 20 mg/day, given over several months.

Lorazepam treatment was started at 1 mg b.i.d., and the dose was gradually raised to 5 mg q.i.d. Mr. A gradually responded with more spontaneous speech, even initiating some conversations. He ambulated alone, maintained eye contact, and completed his activities of daily living, all of which represented a remarkable improvement. He also revealed the paranoid content of his delusional system. Treatment with *d*-amphetamine sulfate, 10 mg p.o. each morning and noontime, led to further activity and increase in speech. The benefits of this combination persisted without evidence of tolerance. During this time he was not being treated with any other psychotropic.

Reduction of the dose of lorazepam while a steady dose of *d*-amphetamine sulfate was maintained was followed by reversion to his former mute and catatonic behavior. We attempted to switch to a comparable dose of clonazepam (up to 4 mg b.i.d. given for 1 week), but Mr. A failed to improve. When placed again on a regimen of lorazepam, 5 mg q.i.d., he responded favorably.

This case demonstrates a significant response of chronic catatonia to a high dose of lorazepam, but not to imipramine, haloperidol, fluoxetine, or clonazepam. It suggests the need for additional research to elucidate the role of benzodiazepines in the management of catatonic schizophrenia, with special attention given to lorazepam (1, 2).

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Seizures During Clozapine Therapy

SIR: Haller and Binder (1) described three patients who experienced seizures during clozapine therapy. We have treated 36 schizophrenic patients with clozapine under experimental protocols; three have experienced major motor seizures. We describe two of these cases.

Ms. A, a 48-year-old, 132-lb woman in good physical health, experienced a witnessed 8-minute grand mal convulsion 10 months after starting to take clozapine. At that time, she had been receiving 900 mg/day of clozapine for 6 months. Clozapine was discontinued and there were no further seizures. A workup, including head CT scan, produced negative findings; an EEG done 3 days after the seizure was unremarkable. As the patient had benefited significantly from clozapine and worsened without it, the drug was restarted 10 days after the seizure, and the dose was gradually increased to 500 mg/day. She was discharged taking that dose and did not require anticonvulsants. She has continued to do well while taking clozapine and has now been free of seizures for more than 3 years.

Ms. B, a 26-year-old, 114-lb woman, had been taking clozapine for just over a month when she experienced a convulsion. She had been in relatively good physical health

except for a history of severe tardive dyskinesia (which improved when she was taking clozapine) and a concussion in an automobile accident 9 years previously. There had been no evident neurologic sequelae of the concussion, and skull films and an EEG were normal. The patient's clozapine dose had been titrated to 900 mg/day within 25 days of her starting to take the drug. Twelve days later, she experienced a witnessed grand mal convulsion lasting 2 minutes; a second convulsion occurred 2 hours later. Laboratory evaluation, including head CT scan, was unremarkable. An EEG the next day revealed diffuse slow wave changes without focal abnormalities. Phenytoin was started and clozapine was discontinued. Despite haloperidol treatment, Ms. B became much more psychotic and refused to eat or drink. Clozapine was reinstituted 9 days after the seizures, and the dose was titrated over a month to 500 mg/day. Phenytoin was discontinued 21 days after the seizures. The patient has remained on a regimen of clozapine, 500 mg day, is doing well in the community, and has remained free of seizures for almost 4 years.

Haller and Binder (1) and others (2) have suggested that clozapine-induced seizures are dose dependent; our experience supports this. We agree with the suggestion that doses over 600 mg/day be used only with careful thought and the anticipation of high seizure risk. In accord with an experimental protocol, Ms. A's and Ms. B's daily clozapine doses had reached 900 mg within a month. Subsequently, both patients had equivalent relief of symptoms with a lesser dose of clozapine. We now prefer very slow upward titration of the dose of clozapine, especially since improvement may occur more slowly than with conventional antipsychotics (3) and because seizure risk may correspond to both dose and rate of increase (2). For patients maintained on clozapine after a seizure, Haller and Binder suggest dose reduction and concomitant anticonvulsant treatment. We suggest that if the patient can be maintained at a substantially reduced clozapine dosage, the inconvenience and risks of anticonvulsant treatment can be avoided. None of our patients has experienced recurrent seizures, including the two patients who have continued to take reduced doses of clozapine for several years without concomitant anticonvulsants.

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Severe Immune Thrombocytopenia Induced by Neuroleptics

SIR: Thrombocytopenia is an uncommon side effect of psychotropic drugs (1-4). Decreased platelet production or increased peripheral destruction have been given as explanations for the pathogenesis of drug-induced thrombocytopenia. We recently observed the following case.

Ms. A, a 24-year-old woman, had shown since age 15, following sexual violence, psychopathologic symptoms

characterized by auditory hallucinations, ideas of reference, delusions, and persecutory trends, which underwent partial and transient spontaneous remission. She was admitted to the hospital because of recurrence of symptoms and started receiving haloperidol, 7.5 mg/day, lorazepam, 7.5 mg/day, and levopromazine, 200 mg/day; she showed significant improvement.

Three months later she developed subconjunctival and skin hemorrhages and epistaxis. Laboratory data revealed a platelet count of 2000/mm³. Bone marrow aspiration showed only a few young megakaryocytes. Treatment with prednisone, 80 mg/day, was started, and psychotropic drug therapy was discontinued. Six days later her platelet count was 8000/mm³, and her psychopathologic condition had deteriorated.

Diazepam, 600 mg/day, was initiated. Because of the lack of significant improvement, the patient underwent a splenectomy, and her platelet count increased to 30,000/mm³. Then azathioprine, 100 mg/day, was initiated, and within 2 months the platelet count had increased to 300,000/mm³.

Meanwhile, because of the recurrence of psychotic symptoms, Ms. A received haloperidol, 9 mg/day, and improved psychiatrically. Azathioprine was then discontinued, and after 10 days the platelet count fell to 45,000/mm³. When azathioprine was restarted, the platelet count increased to 300,000/mm³ within 2 months.

In this case haloperidol and levopromazine produced severe thrombocytopenia that remained unchanged in spite of both medical-surgical therapy and discontinuation of drugs. The patient's platelet count increased significantly only after initiation of azathioprine therapy and remained stable although the patient was restarted on haloperidol. Her platelet count then fell again following discontinuation of azathioprine but gradually improved after new exposure to azathioprine. This supports the hypothesis of drug-induced "immune thrombocytopenia." As far as we know, an isolated immune thrombocytopenia due to neuroleptics has not been previously reported.

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Retinopathy and Bright Light Therapy

SIR: Artificial bright light is increasingly used as therapy for seasonal affective disorder (1) and premenstrual syndrome (2) and has potential use for resetting the biological clock to combat symptoms of jet lag, shift work, and certain sleep disorders (3). The therapy brings with it, however, a risk of permanent eye damage (4). Although there have been no reports of either short- or long-term damage with the use of phototherapy (5), light intensities of the order of 2000 lux, if viewed directly for sustained periods, may damage the susceptible eye.

The need for caution when selecting patients and the advisability of ocular assessment before treatment are illustrated by the following case.

Ms. A, a 42-year-old woman, had a history of postnatal depression after the births of each of her three children (now aged 14 years, 2 years, and 17 months). She required hospitalization and antidepressant medication on each occasion.

Although her postnatal depression improved with tranylcypromine, she then began to notice premenstrual depression, which she described as incapacitating. Each month, during the 10 premenstrual days, she would become progressively more irritable and depressed, sometimes with suicidal ideation. Her abusive outbursts severely strained her marriage. Attempts to suppress the menstrual cycle by continuous use of oral contraceptive pills and later by danazol were not continued because of side effects.

In view of recent reports of successful response to light therapy (2), it was decided to assess this treatment. Although our patient had no history of previous eye complaints, she was referred for extensive ophthalmological screening, as recommended by Terman et al. (5). Ophthalmoscopy revealed a perimacular vertical-pigment epithelial scar, resembling a healed central serous retinopathy, in the left eye. Although the patient was totally asymptomatic, a paracentral field defect could be demonstrated with an Anslar grid chart. Light therapy was therefore contraindicated.

We strongly recommend that ophthalmological investigation be mandatory in all forms of light therapy, even when there is no history of eye complaint, for the following reasons. 1) Artificial light of the brightness used in light therapy could exacerbate any existing retinopathy, and 2) eye damage discovered subsequent to light therapy could be wrongly attributed to the treatment.

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Family Histories of Bulimic Women With and Without Comorbid Alcohol Abuse or Dependence

SIR: Bulik (1) presented data comparing the family histories of drug and alcohol abuse of 35 women who met the *DSM-III* criteria for bulimia with those of 35 normal control subjects.

In this sample, 49% of the bulimic women and 8.6% of the control subjects met the *DSM-III* criteria for alcohol abuse. Alcoholism was the most commonly reported diagnosis for first- and second-degree relatives, with 60% of the bulimic sample (versus 20% of the control subjects) reporting at least one relative with alcoholism. Several other studies have documented high rates of both comorbid and familial psychoactive substance use disorders in women with bulimia and their family members (2-4). Mitchell et al. (5) have shown that bulimic women with positive and negative family histories of psychoactive substance use disorders differ little in terms of clinical characteristics of bulimia, but that those with positive family histories are more likely to have experienced drug problems themselves.

It has become increasingly important, especially with regard to treatment approaches and outcome, to determine how individuals with comorbid eating disorders and psychoactive substance use disorders differ from individuals with eating disorders alone. I therefore examined differences in family psychiatric history of alcohol and drug abuse between bulimic women from the study cited above who reported comorbid alcohol abuse or dependence (group A; N=17) and those who reported no comorbid alcohol use disorders (group B; N=18).

The two subgroups did not differ significantly in age, height, weight, education level, or socioeconomic status. The women in group B provided adequate information for diagnosis of an average of 8.1 relatives, and the women in group A reported on an average of 7.9 relatives ($t=0.72$, $df=33$, n.s.). Family history data were gathered by using the Family History Research Diagnostic Criteria semistructured interview. The results were dichotomized into 1) no first- or second-degree relatives or 2) one or more first- or second-degree relatives with drug or alcohol abuse or dependence.

Of the 18 group B subjects, nine (50%) reported no relatives and nine (50%) reported one or more relatives with alcohol or drug abuse or dependence. Of the 17 subjects in group A, four (23.5%) reported no relatives and 13 (76.5%) reported one or more relatives with alcohol or drug abuse or dependence. The odds ratio was 3.25 (95% confidence interval=0.76-13.91), indicating that bulimic women with comorbid alcohol abuse or dependence were more likely to have a family member with a psychoactive substance use disorder. However, the risk was not significantly greater, possibly because of the small sample size and hence low power (0.37) of the study.

A more detailed understanding of the differences between bulimic individuals with and without comorbid psychoactive substance use disorders—in terms of the clinical characteristics of the eating disorder and the substance use disorder, the nature of the familial alcoholism (e.g., gender of those afflicted; type I or type II disorder), and the longitudinal course and outcome of both disorders—could aid in determining which alternative approaches are preferred in dealing with the patient who has both diagnoses.

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Methadone Dose for Cocaine Abuse

SIR: It is well-known that cocaine abuse is a major problem among methadone-maintained opiate addicts. There is some evidence that methadone maintenance can exacerbate cocaine abuse in this population (1). However, administration of morphine has been shown to suppress self-administration of cocaine in squirrel monkeys (2). There is also recent evidence that the opiate agonist/antagonist buprenorphine can be an effective treatment for cocaine abuse (3). The mechanism of buprenorphine action is not clear, although it is proposed that the opiate agonist component or the agonist/antagonist combination (as opposed to the antagonist action) is critical for the effects on cocaine self-administration (3). The effect of methadone dose itself in cocaine abuse is therefore an important question.

We have developed a contingency treatment program in which a methadone-maintained patient's dose depends on the patient's cocaine abuse (as determined by urine screen). Specifically, in this protocol, the patient's methadone dose is increased by 5 mg in response to each cocaine-positive urine screen, to a maximum dose of 120 mg/day.

Six patients have entered this protocol to date, and all six responded to this treatment by stopping cocaine abuse. The average patient was 35 years old and had a 3-month documented history of cocaine use (5.5 times per week). The average methadone dose at which abstinence was achieved was 115 mg/day. Urine screens were obtained one or two times per week. The average number of urine screens (at a methadone dose of 70 mg) was eight. Eighty-one percent of these were positive for cocaine. Of urine screens obtained after initiation of a methadone dose increase (average of 13 urine samples per subject), 40% were positive for cocaine. Furthermore, a precipitous decline in cocaine use at higher doses of methadone was observed. Of urine screens obtained (average of eight per subject) after maximum methadone dose was reached (average of 115 mg), 10.8% were positive for cocaine. The mean duration of abstinence was 8 weeks (range=3-10 weeks). At 3-month follow-up, four patients remained abstinent, and two had left the program for other reasons.

These results suggest that a methadone dose contingency treatment program, which increases methadone dose in response to cocaine abuse, may be successful in treating cocaine abuse in methadone programs. This finding is especially significant in view of the fact that most methadone programs respond to cocaine abuse by lowering the methadone dose or "detoxing" the patient from the program as a disciplinary action. It is possible that this response actually increases the biological tendency toward cocaine use.

We recommend further study of the interaction of methadone dose and cocaine abuse.

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Tranlycypromine Abuse

SIR: The monoamine oxidase inhibitor tranlycypromine is useful in the treatment of several psychiatric disorders, but information about the abuse potential of this medication is sparse. We report a case of tranlycypromine abuse.

Mr. A, a 35-year-old white man, was referred for treatment of anxiety and depressive symptoms. He had a 3-year history of generalized anxiety with excessive worry, chest tightness and palpitations, muscle tension, tremulousness, headache, and chronic dysthymia. He had a history of CNS stimulant and sedative-hypnotic abuse: *d*-amphetamine, 30-50 mg/day; diazepam, 30-60 mg/day; secobarbital sodium, 200-400 mg/day; and alprazolam, 8-12 mg/day, in varying combinations over 7 years. He had been hospitalized in the past for sedative-hypnotic dependence. He stated that he felt as if he had been "in withdrawal" for the past 3 years but had not been abusing any drugs during that time. His family psychiatric and substance abuse history was negative.

He had been treated with buspirone, trazodone, and imipramine, all of which had been discontinued because of side effects. A diagnosis of dysthymia and generalized anxiety disorder with narcissistic personality traits was made. Treatment with tranlycypromine in doses gradually increasing to 40 mg/day was instituted. The patient had a dramatic response to this regimen; he reported improved mood and productivity and a reduction in anxiety symptoms and headache. The only adverse effect was hypsomnia.

Three weeks later Mr. A was found delirious and incoherent in his home by his sister. Physical and neurological examinations produced normal findings. He was hospitalized for evaluation, and a toxic screen (plasma and urine) showed only tranlycypromine, 6 ng/ml (36 hours after his last dose), and caffeine. No drugs of abuse were located in his home. He recovered in 24 hours and reported that he had been drinking 20 caffeinated beverages a day because of daytime fatigue; he attributed his delirium to lack of sleep and caffeine abuse. Tranlycypromine was resumed, and 3 weeks later he was again found wandering nude and delirious. Again, toxic screens revealed tranlycypromine only. A search of his home revealed several empty tranlycypromine prescription bottles, all from different physicians. He subsequently admitted to rapidly escalating the dose of the drug because of the stimulant-like effects and taking an average of 300 mg/day after the first 2 weeks of treatment. He denied any other current drug or alcohol use. He requested that the medication be continued at this dosage despite the obvious complications. He was referred for intensive substance abuse treatment.

In prior reports of tranlycypromine abuse (1-3), all patients had histories of alcohol abuse and sometimes polysubstance abuse. The capacity of tranlycypromine to exert amphetamine-like effects has been reported (4).

mine-like effects presynaptically and its minor metabolic pathway to amphetamine (4) may help to explain its abuse potential. It is possible that stimulant abuse predisposes to tranylcypromine abuse. In light of the current cocaine epidemic, it may be that evaluation for previous substance abuse and closer monitoring of prescriptions for tranylcypromine are indicated.

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Effects of Smoking Cessation on Serum Neuroleptic Levels

SIR: The Environmental Protection Agency's preliminary report classifies passive cigarette smoke as a class A carcinogen, in the same category as asbestos, radon, and benzene. Recent epidemiological data suggest that passive smoking causes about 50,000 deaths a year (1). "As data emerge that show the effects of passive smoking on long- and short-term morbidity, highly visible smoking in health care settings has become logically inconsistent with the health goals of medical institutions" (2). Amidst the increasing concerns about passive smoking, individuals appear to be under greater pressure to stop smoking. This raises a concern regarding smoking cessation by patients taking neuroleptics, because smoking cessation may increase neuroleptic serum levels, placing patients at greater risk of neuroleptic adverse effects.

Some of the evidence for this assertion is as follows: "Cigarette smoking has been found to be associated with a 2.33-fold increase in the clearance of fluphenazine decanoate" (3). "Smokers had significantly lower haloperidol and reduced haloperidol plasma concentrations than nonsmokers ($p < 0.01$, $p < 0.05$)" (4). Current data suggest that tobacco smoke lowers neuroleptic plasma levels. This probably occurs through the polycyclic aromatic hydrocarbons in cigarette smoke inducing the hepatic enzyme cytochrome P448 (5). In contrast to the effects of smoke exposure, smoking cessation probably decreases hepatic enzymatic induction, thus significantly raising neuroleptic plasma levels and consequently placing the patient at risk of increased side effects. This is supported by a case report: "Presence and severity of adverse effects and chlorpromazine plasma levels correlated directly with tobacco smoking over a 16-month period" (5).

In consideration of Environmental Protection Agency reports and new epidemiological data, the current trend toward containment and abatement of cigarette smoking may escalate. Consequently, more and more patients taking neuroleptics may change their smoking behavior, placing them at increased risk of adverse neuroleptic effects. During these times of mounting pressure for smoking cessation, care in monitoring neuroleptic side effects is urged.

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Smoke-Free Hospital Environments in 1848

SIR: Like many hospitals across the country, Ohio State University Hospitals in Columbus, Ohio, adopted a "modern, progressive" smoke-free policy on March 31, 1991. This policy also affected the psychiatric facility. The medical and ethical aspects of this decision had been extensively discussed by faculty and staff.

I believe *Journal* readers might be interested, as I was, in Dr. Pliny Earle's comments on tobacco, which were written almost a century and a half ago. Dr. Earle was superintendent of the Bloomingdale Asylum in New York and one of the 13 founders of the organization that later became the American Psychiatric Association (1).

In an article that appeared in the *American Journal of Insanity* in 1848 (2), Dr. Earle was very critical of the effects of tobacco and stated his belief that it could aggravate different forms of mental illness. This being the case, he concluded, "its action, upon the whole, is considered so deleterious, that in most of the well conducted establishments for the insane in this country, its use among the patients is prohibited. At this institution it is not permitted, excepting in a few cases, in small quantities, by patients who have resided here many years."

History does not necessarily repeat itself, but it appears to have done so in this instance.

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Pilot Program of Treatment for PTSD

SIR: There is a subset of Vietnam combat veterans with chronic posttraumatic stress disorder (PTSD) who appear refractory to ordinary treatment modalities. Among the symptoms that interfere with their involvement in therapy are lack of trust, interpersonal isolation, and intense and sometimes eruptive rage, frequently complicated by a prolonged history of alcohol/drug abuse. The persistence of emotional and behavioral difficulties, unrelieved in some men for over 20 years, has prompted the Department of Veterans Affairs to devise

nationwide, multimodal treatment approaches. A major therapeutic challenge is that of encouraging patients' compliance with treatment efforts over time. This report describes a medication regimen, started in our New Orleans facility, that has been observed to afford both prompt relief of symptoms and sustained commitment to a multimodality team approach incorporating psychotherapeutic groups, individual psychotherapy, and family therapies.

Successive outpatients enrolled in the specialized PTSD clinic team program (N=158) were followed by the multidisciplinary treatment team for 12 months. All of the patients were free of psychosis and were free of drugs and alcohol for 30 days before treatment was initiated. Among the treatment modalities were cognitive-behavioral and psychodynamic psychotherapy, crisis intervention counseling, and psychotropic medications tailored to the veterans' individual needs. The psychotropic regimen consisted of an initial combination at bedtime of fluoxetine, 20 mg/day, with amitriptyline, 50 mg, or an equivalent tricyclic antidepressant and clonazepam, 0.5–1 mg. Eighty-six percent (N=136) of the men remained involved in group, individual, and family therapy at 6-month follow-up. Thirteen men required brief hospitalization for acute exacerbation of PTSD, and 19 were lost to follow-up. Fifty-four men were found to have histories of drug and/or alcohol abuse, and 34 reported previous psychiatric hospitalizations.

Patients' reports verified separately by three clinicians suggest 48–72-hour relief of persistent hyperarousal symptoms, including insomnia, nightmares of combat, and flashbacks. Simultaneously, patients began to attain therapeutic blood levels of antidepressant with low doses of tricyclic and fluoxetine, without the unacceptable side effects of higher tricyclic doses (1–3). Treatment appeared to become effective against depressive symptoms within 3–8 weeks. Medications were monitored by the psychiatrist on a monthly basis for 6 months on average until a stable clinical situation prevailed. The combination of medications was well tolerated with few side effects, none of which was lasting. One patient developed a generalized skin rash after 30 days, and six men complained of erectile and ejaculatory delay but no true impotence. One veteran experienced a brief confusional state. Another patient, who had comorbid severe depression, PTSD, and alcoholism, attained the high blood level of 794 ng of amitriptyline after attempting suicide with an overdose. He was referred for detoxification and survived without ill effect. These problems raise important questions about the need for careful medical monitoring.

Despite these adverse experiences, the observed tendency for prompt relief of chronic painful, debilitating symptoms by this combination of medicines may permit development of a more durable doctor-patient relationship as well as an opportunity to begin to address the psychological sequelae associated with extreme trauma. Importantly, the patient's sense of hope in therapy may be rekindled after many years of inadequate and frustrating experiences in the treatment situation. Such clinically derived conclusions, however, suggest the need for double-blind, placebo-controlled studies of these medications individually and in combination to determine their true efficacy.

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Carbamazepine, Lithium, and Life Course of Bipolar Affective Disorder

SIR: Carbamazepine alone (1) and in combination with lithium (2) is effective in the acute and prophylactic treatment of patients with bipolar affective disorder who have failed to respond to lithium. Although it has been suggested that patients with rapid cycling are more likely to respond to carbamazepine (1), careful attention has not been paid to the life course of illness of patients who respond to lithium, carbamazepine, and the combination of these two treatments. I therefore carried out a careful clinical evaluation of life course of illness in patients sequentially treated with lithium, carbamazepine, and the combination.

Life course of illness was evaluated in 43 subjects with primary bipolar affective disorder followed in the Mood Disorders Program at the University of Toronto by a method previously described (3). Lithium was prescribed in doses of 900–1800 mg/day to achieve blood levels of 0.7–1.0 nmol/liter. Carbamazepine was used in doses of 600–1600 mg/day, with therapeutic blood levels reached in all cases. Response to a particular treatment was defined as resolution of the acute affective episode for which the treatment was prescribed and/or complete absence of affective episodes for a minimum of 1 year. Since acute treatment involved use of benzodiazepines or neuroleptics in some cases, this was really an assessment of response to maintenance medication. Patients were defined according to their life course of illness as rapid cyclers (four or more affective episodes in a 12-month period), normal cyclers, and continuous cyclers (persistent fluctuations between mania and depression with no prolonged or sustained periods of normal mood).

Twenty-five subjects responded to lithium, 11 responded to carbamazepine, and seven responded to the combination administered in sequential fashion. Of the 25 lithium responders, 22 were regular cyclers, two were rapid cyclers, and one was a continuous cyler. Of the 11 carbamazepine responders, eight were rapid and three were regular cyclers. Of the seven who responded to the combination, two were regular and five were continuous cyclers.

My careful clinical evaluation confirms earlier impressions that carbamazepine responders tend to have rapid cycling, whereas lithium responders have regular cycles of bipolar disorder. Of particular note was the finding that responders to combined lithium and carbamazepine were predominantly characterized by continuous mood cycles. This was not an attempt to carry out a controlled study but, rather, to provide a careful systematic clinical evaluation of life course of illness in relation to treatment response, subject to the limitations of the sequential treatment used. These observations are preliminary because of the clinical nature of the data collection and require clarification in a randomized, double-blind study of the acute and prophylactic efficacy of these treatments.

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Cardiac Transplantation and Depression

SIR: Refinement of surgical and anesthetic techniques, improved selection of transplantation candidates, and the introduction of cyclosporine have resulted in a significant increase in both the number and survival of cardiac transplantation patients (1). A parallel rise has occurred in delayed postoperative psychiatric complications, particularly depression (1, 2). Treatment for these episodes typically involves psychotherapy and antidepressants, with occasional conjoint use of psychostimulants. However, a MEDLINE search of the literature revealed no reports on the use of ECT. I wish to report the successful treatment with ECT of a patient with a major depressive episode after cardiac transplantation.

Mr. A was a 61-year-old white man who, 6 months after cardiac transplantation, presented with a breakthrough episode of *DSM-III* bipolar disorder, depressed type, while on a maintenance regimen of amoxapine, 150 mg nightly, and methylphenidate, 5 mg b.i.d. At admission his score on the Hamilton Rating Scale for Depression was 34. He showed extreme anorexia and clinical deterioration. A reevaluation by the transplant team indicated stable graft function with life-threatening malnutrition and dehydration, which abrogated further medication trials. Following clinical stabilization of the patient, a decision was made to proceed with ECT.

Before ECT, Mr. A was evaluated with a physical examination, a serum chemistry screen, urinalysis, an ECG with rhythm strip, chest X-ray, cranial CT scan, a cervical and thoracic spine series, and sequential checks of vital signs. He received seven treatments of bilateral ECT administered with a Medcraft model B24-III machine and standard temporofrontal placement. Prestimulus preparation consisted of 40 mg i.v. of methohexital, sphynomanometric isolation of the left upper extremity, 50 mg i.v. of succinylcholine, and preoxygenation with 100% oxygen through a face mask, which was continued through posttreatment recovery. One hundred ten volts of pulse wave current were applied for 0.5 second per treatment, with the resultant tonic-clonic seizure timed by monitoring of the left upper extremity. Cardiac status was monitored by a 12-lead ECG monitor, a pulse oximeter, and serial blood pressure measurements before treatment, immediately after seizure, and repeatedly until full recovery. Pretreatment blood pressure averaged 170/110 mm Hg; pulse, 96 bpm. Peak posttreatment blood pressure averaged 220/138 mm Hg; pulse, 130 bpm, responsive to 5 mg i.v. of labetalol after seizure. The patient experienced no other cardiac complications from ECT. Post-ECT ECGs revealed no change from admission status.

Mr. A did experience post-ECT confusion characterized by a decrease in his Mini-Mental State examination score for 6 days following treatment. His score decreased from 28 on admission to 19, with spontaneous recovery to a final score of 28. His Hamilton depression score improved to 9. He was discharged to follow-up on a regimen of amoxapine, 100 mg nightly.

Although the vagal denervation resulting from cardiac transplantation obviates the risk of immediate postseizure bradycardia, clinical concern regarding the subsequent sympathetic discharge, with its attendant tachycardia and pressor response (3), may have contributed to the dearth of reported cases of use of ECT in this special population. Despite the possibility of these and other cardiac complications, however, ECT has been well tolerated by other types of cardiac patients (3-5). This case indicates that ECT may be well tolerated in cardiac transplantation patients as well. Larger samples must be obtained to support further generalizations about the use of ECT in this population.

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Capgras' Syndrome in a Blind Patient

SIR: Lately, most reports and articles about Capgras' syndrome have emphasized the importance of organic factors in its etiology, and many authors (1, 2) hypothesize that an alteration in the visual routes of facial recognition plays an important role in it. We have seen a blind patient who suffered a delusion of doubles, in whom such an alteration seemed not to be an important etiopathogenic factor.

Mr. A was a 32-year-old man who had a 12-year history of insulin-dependent diabetes mellitus. He had suffered a diabetic retinopathy and had been completely blind for 3 years. He had no psychiatric history. He was admitted to the hospital in a hypoglycemic coma and was treated with intravenous glucose. While recovering from the coma, he developed haptic and visual hallucinations of little animals and experienced temporospatial disorientation. An EEG showed signs of metabolic encephalopathy; a CT scan was normal. Treatment with haloperidol, 5 mg/day, was started, and in a week the hallucinations disappeared and consciousness was normal, but the patient began to express the conviction that a double had been substituted for his mother. At that time his mother was not at the hospital, and

she visited him only several days later. When Mr. A touched her hand, he said that she was not his mother but a double, because the skin of her hand felt softer. The findings of a neuropsychological examination were normal; there was no tactile agnosia. Haloperidol was continued, and the delusion disappeared in 15 days, with complete return of the patient to his normal life.

Because of his physical condition, Mr. A had been absolutely dependent on his mother for many years. One week before he was admitted to the hospital, he had an argument with his mother. To show his anger, he did not talk to her, did not follow his diet, and took medication in an uncontrolled way, which finally resulted in the hypoglycemic coma.

Our patient suffered a metabolic encephalopathy probably due to diabetic decompensation and hypoglycemia, which was the likely cause of the delusional syndrome. There is a similar case in the literature (3). Mr. A had ambivalent feelings about his mother and, as Berson (4) suggested, pathological splitting could have played a role in the formation of the delusion.

The fact that Capgras' syndrome appeared in a blind patient (we have found no published case in the literature, but only the mention of a blind patient with a delusion of doubles [5]) suggests that the delusion does not always result from an alteration in pathways of facial recognition. As Signer (5) pointed out, perceptual phenomena could have played a secondary role in our patient's delusion.

Capgras' syndrome seems to be a multidetermined phenomenon in which a destructuring of thought processes, probably organically based, modeled by dynamic factors, brings about the delusional belief in a double. Perceptual alterations in our patient seemed to play a secondary role, although we cannot say that they were not necessary.

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Rapid Cycling in a Patient With Bipolar Mood Disorder Secondary to Graves' Disease

SIR: Several clinical studies indicate that hypothyroidism during bipolar illness is a risk factor for the development of rapid cycling (1). Also, rapid cycling bipolar patients have a high prevalence of hypothyroidism. We wish to report, however, the case of a patient with bipolar mood disorder who developed rapid cycling secondary to hyperthyroidism.

Mr. A, a 47-year-old white, married man with a 7-year documented history of bipolar mood disorder, had been

maintained on a lithium regimen. He was admitted to our unit in an acute manic phase, which was his sixth episode that year. His physical examination at admission revealed that all of his deep tendon reflexes were brisk and hyperactive, which made us suspect a possible hyperthyroid state. His records showed good compliance with the lithium regimen, therapeutic blood levels, and normal thyroid tests when he was checked at 6-month intervals. Previous to that year, Mr. A had had a cyclic pattern of depressed episodes characterized by hypersomnia, marked decrease in productivity at work, and intense suicidal ideation, which would be followed by episodes of hyperactivity, decreased need for sleep, and overspending sprees, with never more than four major mood swings per year (2).

At admission Mr. A's thyrotropin level was 0.00 IU/ml. His serum T_4 level by radioimmunoassay, T_3 resin uptake, and calculated free T_4 index were all elevated. These values were confirmed by a T_3 assay. Given prior clinical impressions that thyroid function testing alone does not predict the severity of thyroid disease (3) and the fact that lithium therapy could have played a role in masking a preexisting hyperthyroid state, a thyroid scan was obtained, which was consistent with Graves' disease (diffuse goiter). Since Graves' disease is less common in males, and Mr. A had a negative family history of thyroid disease, an endocrinology consultation was obtained. We followed the recommendation to treat Mr. A with a single dose of iodine-131 radiation therapy. Following completion of treatment, his acute manic episode subsided. He was maintained on a lithium regimen and discharged to outpatient follow-up. For the 4 subsequent months, he continued to be euthymic and has not relapsed into a rapid cycling pattern.

The influence of thyroid hormones on the CNS has been recognized since the first description of a clinical deficiency of these hormones in 1873 by Sir William Gull (4). Whybrow and Prange (5) suggested that "thyroid hormones play an important role in modulating catecholamine neurotransmission in the CNS and this may serve as a mechanism of physiologic adjustment or defense during times of adaptive demands." The hypothesis that relative CNS thyroid hormone deficiency during bipolar illness leads to rapid cycling appears to be of heuristic value in that it accounts both for the high rates of hypothyroidism among rapid cycling patients and for the clinical efficacy of exogenous thyroid hormone administration in the absence of preexisting hypothyroidism (1). A lack of thyroid hormones can lower the threshold for depression; an excess can contribute to a state of tense dysphoria (5). We hypothesize that the development of Graves' disease in patients with preexisting bipolar disorder may lead to an excess mobilization of thyroid hormones and to an increased vulnerability for rapid cycling. To test this hypothesis further, more clinical investigations will be required.

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The Judges Don't Want To Do It Either

SIR: In a previous letter (1) I reported an unsuccessful attempt during the 1989 Oregon legislature to link proposed legislation articulating the duty to protect with an omnibus gun control bill. In this letter I write to inform readers of another interesting aspect of the 1989 Oregon gun control legislation.

The 1989 legislation prohibited specific groups, including persons who were civilly committed, from purchasing handguns. It was agreed that queries would be made of the Oregon Mental Health Division about whether an individual attempting to purchase a handgun had been civilly committed in the 4 years prior to the enactment of the law. If on the list, an individual would be prohibited from purchasing a gun.

Intense debate focused on how to limit gun purchases by individuals who were committed after the law went into effect. A suggestion by the Oregon Psychiatric Association was adopted, which required the trial court judge who committed the individual to determine whether the individual would be allowed to purchase a gun at some point in the future. The Oregon Psychiatric Association's position was that the trial court judge was in the best position to make this decision, after having heard the evidence made available at the commitment hearing and having made the decision to commit the person. This provision was codified into statute as follows:

[The court] shall order that the person be prohibited from purchasing or possessing a firearm if, in the opinion of the court, the prohibition is necessary as a result of the person's mental or psychological state as demonstrated by a past pattern of behavior or participation in incidents involving unlawful violence, or by reason of a single incident of extreme violent, unlawful conduct. (2)

This statute has been in existence for a full year, and to date the judges have entered orders prohibiting the purchase of firearms in 28 cases (1.7%) out of approximately 1,675 commitments per year in Oregon. Why have the judges found so few civilly committed patients unfit to own guns? The answer awaits empirical testing, but several possible explanations come to mind. 1) The statute to deny purchase is restrictive, and a rate of 1.7% may accurately reflect the limits imposed by this statute. 2) Not enough time has passed, and the judges are not generally familiar with this new statutory responsibility. 3) The judges don't want to predict dangerousness. Psychiatrists are said to overpredict dangerousness because of fears of liability. Can we hypothesize that judges are underpredicting because of the political liabilities of gun control and fears of being labeled as favoring limits to gun ownership? In Oregon, judges are elected in contested elections.

We support the system of having judges rather than psychiatrists predict dangerousness. We bring this approach to the reader's attention as interest in gun control grows. It will be interesting to follow this situation as it matures.

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Holding the Center: The Medical Implications of the *Cruzan* Decision

SIR: The refusal of life supports has now obtained constitutional support with the decision by the U.S. Supreme Court in the *Cruzan* case (1). The Supreme Court has embraced each competent individual's right to refuse medical treatments on the basis of Fourteenth Amendment liberty interests. The Court has also indicated that the state of Missouri or any other state has a right to demand clear and convincing evidence of an incompetent patient's prior wishes. This has led to an increased interest in living wills and durable powers of attorney. The prevailing sentiment is that a patient's prior wishes should be honored and that family members are best able to do this. If one reads the body of *Cruzan*, there is no sense of a role for physicians in this process, and at a recent meeting on Medical Decision-Making and the "Right to Die" After *Cruzan*, held in Washington, the participants viewed physicians as part of the problem rather than part of the solution.

There are several reasons, however, to look with a cold eye at the psychological issues involved in living wills and durable powers and at the capacity of families to make objective decisions for dying members. Let us recall that in the case of Carrie Coons (2), an 86-year-old woman who presumably had given concrete evidence regarding what she would wish to have done if she were in a persistent vegetative state, when she awakened from that state was no longer so sure about what she wanted done. This addresses the problem of making a future decision based on a legal document drawn up at one point in time. People's wishes change, situations become complicated, and living wills and durable powers of attorney really cannot keep pace with human flexibility and conflict. In addition, families, while often helpful, are subject to conflict, bias (both conscious and unconscious), and disagreements, which can compromise their effectiveness in making decisions about life supports.

It is my contention that the best database for making a decision about termination of life support is a medical record over a longer period of time that documents the physician's conversations with the patient. This avoids the one-point-in-time problem and also avoids some of the family biases, as well as problems caused by the absence of families in some of these cases. This has implications, of course, for medical education. Doctors need to be taught and retaught how to talk to younger and older patients about death. They need to be able to deal with their own conflicting feelings about the subject. Doctors need to emerge as the leaders in a complicated group that includes family, nurses, friends, and the patient in making decisions to terminate life support. If this does not happen, we shall find that the core of being a physician, which involves helping a sick person, will have been transferred from doctors to lawyers and families. In my opinion, this would be a disastrous occurrence. I therefore urge all teachers of interns, residents, and physicians to incorporate as part of the standard medical history an ongoing documented and persistent investigation of the patient's wishes about life support.

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Meaning of the Term "Bulimia"

SIR: Albert Stunkard, M.D., presented the translation of a description of bulimic patients by M. Wulff in 1932 (1) and, referring also to earlier case descriptions, argued for the historical continuity of "bulimia." Although the reconstruction of the historical development of syndromes suffers from having a weak database, it is nevertheless a possible and meritorious argument.

My comment concerns the meaning of the term "bulimia," an issue that Dr. Stunkard did not directly address. If bulimia is to mean some form of neurotic, impulsive overeating, then the assumption of historical continuity is plausible. Used in this sense, bulimia was described up to the end of the nineteenth century, usually grouped together with polyphagia, pica, and anorexia (i.e., loss of appetite) as disorders of the appetite; they are present in a large portion of books on internal medicine, especially on gastrointestinal disorders (2). If, in contrast, bulimia is to include cognitions related to body weight and practices such as self-induced vomiting, dieting, etc., as has been the tendency in the 1980s, then it must be considered as a new syndrome, and Wulff's case description of bulimia nervosa must be considered as almost the earliest in history (one patient feared becoming overweight, and two were ashamed of their bodies), since in all other cases referred to by Dr. Stunkard the patients lacked the fear of being or becoming overweight, with the exception, of course, of Janet's one anorexic patient. Historically, in fact, among patients with eating disorders, the fear of being overweight first emerged in the context of anorexia nervosa (3, 4).

The history of bulimia, I would suggest, forces us to acknowledge the plasticity of neurotic symptoms and the historical relativity of attempts to define "syndromes" in a precise manner. Today the symptom of bulimia, or impulsive overeating, usually is organized around the cognition of being relatively overweight, but there are still many cases of patients with the symptom of bulimia that fall into the category of atypical eating disorders. To sum up, I wish to add to Dr. Stunkard's contribution a concern for historically changing combinations of symptoms, which results in considering the symptom of bulimia (overeating) as very old, but makes it clear that weight-related fears, typical for modern bulimia nervosa (and anorexia nervosa), are distinctly modern.

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Dr. Stunkard Replies

SIR: I am indebted to Dr. Habermas for his comments on my article, for his scholarly historical review of the concept of bulimia nervosa, and for his paper (his reference 3), which will be more accessible to non-German-speaking audiences. Dr. Habermas correctly distinguishes between bulimia as bouts of binge eating and the more restricted meaning associated with "bulimia nervosa," which has been closely associated with concerns about body image. His writings provide strong evidence that although bulimia as bouts of impulsive (binge) eating appears to have a long history, bulimia as binge eating with associated body image disturbance and purging behavior is of relatively recent origin. As he suggests, the 1932 paper by Wulff that appeared in translation may well be the first description of this latter disorder.

Recent developments have provided gratifying confirmation of Dr. Habermas's emphasis on the plasticity and changing combinations of neurotic symptoms. For a number of years, binge eating has been considered in the medical literature primarily as a component of bulimia nervosa, in association with disturbed body image and purging. It now appears that binge eating together with body image concerns, but without purging, constitutes a clearly defined clinical entity, with a prevalence as high as 20%-46% of obese persons. A description of this new syndrome should appear shortly (manuscript on binge eating disorder by R.L. Spitzer et al., submitted for publication).

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Dissociative Experiences and Eating Disorders

SIR: We read with interest the findings in the article "Relation of Clinical Variables to Dissociative Phenomena in Eating Disorders" by Mark A. Demitrack, M.D., and associates (1). In a similar study of the relation between dissociative experiences and eating disorders (2), we compared the Dissociative Experiences Scale scores of 25 women with eating disorders to those of a group of 25 age-matched women. Our findings support those reported by Dr. Demitrack and associates that subjects with eating disorders had significantly higher scores. The mean total scale score was 17.8 for the group with eating disorders and 3.7 for the comparison group (Dr. Demitrack and associates reported mean total scale scores of 16.7 and 6.4, respectively). As in the study by Dr. Demitrack and colleagues, our group with eating disorders reported a significantly higher rate of self-mutilation and shoplifting.

We were particularly interested in Dr. Demitrack and associates' discussion of the possible relation of eating disorders and dissociation to childhood sexual abuse. In our study, we investigated the prevalence of childhood sexual abuse in the subjects with eating disorders and in the comparison subjects. The subjects with eating disorders had a significantly higher rate. Furthermore, we categorized the data by the type of sexual abuse, i.e., sexual abuse restricted to touching, oral intercourse, or genital intercourse. The subjects with eating disorders reported significantly higher rates of childhood sexual abuse involving both oral intercourse and genital intercourse. However, there was no statistically significant difference between these subjects and the comparison subjects in reported rates of sexual abuse restricted to touching. These findings suggest that the subjects with eating disorders experienced more severe forms of childhood sexual abuse than did the comparison subjects.

There are a number of possible explanations for the findings of both studies that parallel the multidimensional nature of eating disorders and dissociation. It may be that the high proclivity toward dissociative experience in subjects with eating disorders, found in both studies, is due to physiological compromise induced by metabolic imbalance, nutritional inadequacy, and electrolyte disturbance. However, our finding of a greater prevalence of childhood sexual abuse in those subjects is consistent with Dr. Demitrack and associates' suggestion that patients with eating disorders have often been subjected to traumas which may place them at risk for dissociative psychopathology. The findings in both studies suggest that further investigation of the relation between eating disorders and dissociative experiences is needed in order to gain greater understanding of the etiology and treatment of both of these phenomena.

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Dr. Demitrack and Associates Reply

SIR: We appreciate the comments from Dr. Goldner and colleagues on our recent article and are pleased to note their confirmation of the results of our study. We would also like to add the following comment. As noted in our article, members of our group have examined preliminary data on the incidence of childhood sexual abuse in concurrently assembled groups of patients with eating disorders, general psychiatric patients, and normal female control subjects (1). These data suggest that although the subjects with eating disorders had experienced far more sexual abuse than the normal population (as in Dr. Goldner and associates' study), sexually abusive experiences were no more common for these subjects than in the general psychiatric patients.

These findings, in conjunction with the comments of Dr. Goldner and colleagues, add to a growing body of data suggesting the importance of antecedent childhood trauma as a risk factor in the pathogenesis of adult dissociative psychopathology. It is also becoming clear that these antecedent events may cut across established diagnostic boundaries to produce observable dissociative events.

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MARK A. DEMITRACK, M.D.
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Negative Symptoms in Schizophrenia

SIR: I read with interest the article by Richard R.J. Lewine, Ph.D. (1) on negative symptoms. I would like to add another point which could be helpful in understanding the discriminant validity of negative symptoms.

Negative symptoms have been classically described in schizophrenia but are also seen in depression and certain other disorders. Depression and drug-induced extrapyramidal side effects such as akinesia often mimic negative symptoms. Since depressive symptoms have been seen to occur during various phases of schizophrenia from the prodromal period through the active stage to the residual phase, it is very important to control for these when assessing negative symptoms. Although antipsychotic medication may relieve the depressive symptoms in schizophrenia along with its specific effect on the psychotic symptoms, I have seen in my clinical practice that antidepressant therapy is often helpful in relieving the depressive symptoms of schizophrenic patients after antipsychotics have failed to do so. Since negative symptoms have been found to occur in depressed patients as well (2, 3), and the depressive symptoms occurring as part of schizophrenic illness may also contribute to the negative symptoms, an evaluation of negative symptoms in schizophrenic patients with accompanying depressive features after a course of antidepressants may give a clearer picture and be helpful in studying the discriminant validity of negative symptoms.

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RAKESH K. CHADDA, M.D.
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Dr. Lewine Replies

SIR: Dr. Chadda reminds us of the complex relation between depression and negative symptoms in schizophrenia. As my colleagues and I have pointed out elsewhere (1, 2), the separation of "negative" and "depressive" symptoms is particularly difficult because many of them are operationalized in identical terms, as in the case of anhedonia. There are practical consequences of these confounding clinical factors, since the selection of appropriate pharmacologic agents often depends on how the symptoms are conceptualized. Specifically, if the therapist interprets poverty of speech, anhedonia, and loss of interest as part of a schizophrenia syndrome, then antipsychotics are most likely to be used. In contrast, these same symptoms might be conceptualized by another therapist as part of a depressive syndrome and antidepressants would be prescribed. The original study to which Dr. Chadda refers in his letter was designed specifically to address this problem by looking at the short-term longitudinal course of both negative and depressive symptoms. The data clearly supported the differentiation of negative from depressive symptoms. Negative but not depressive symptoms discriminated the schizophrenic from the nonschizophrenic (largely depressed) patients, and over the course of several months of antipsychotic medication,

depression improved in both psychiatric groups while negative symptoms remained constant in the schizophrenic group but decreased in the nonschizophrenic group.

Configurational analysis is particularly important in differentiating these types of symptoms. Consider, for example, that negative symptoms in male schizophrenic patients tend to be correlated with poor premorbid development, enlarged lateral ventricles, and poor outcome, while in women they tend to be more highly correlated with good premorbid development, presence of depression, and good treatment response (3). The negative symptoms in our discriminant validity study behaved quite differently in the nonschizophrenic, depressed group than they did in the schizophrenic group. Simple statements to the effect that negative symptoms occur in various diagnostic groups are, therefore, somewhat misleading.

Irrespective of how we conceptualize negative and depressive symptoms, a trial of antidepressants in their treatment is always available as a reasonable strategy, as pointed out by Dr. Chadda. I would refer those interested in a sophisticated differential pharmacologic approach to the treatment of negative symptoms to an excellent article by Carpenter et al. (4), in which the authors offer a procedure for systematically assessing symptoms and introducing neuroleptics, anticholinergics, antidepressants, anxiolytics, and various other forms of therapy as indicated. It is incumbent upon us to consider all forms of intervention in treating the symptoms of schizophrenia until such time as we understand better its etiology.

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RICHARD R.J. LEWINE, PH.D.
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Erotomania

SIR: The review "Erotomania Revisited: From Kraepelin to DSM-III-R" (1) serves to perpetuate many of the myths and errors in the literature. The term *psychose passionnelle* referred to in the article was the term de Clérambault used for delusional states that were restricted to a single theme (*en secteur*), with an emphasis on the affective contribution. While best outlined for erotomania, he envisaged similar mechanisms for delusional jealousy and litigiousness as well as hypochondria. Only the five "pure" cases have appeared in partial translation (2), albeit they are without any description of phenomenology. Omitted are the five secondary (or "associated") cases and one "pure" case, as well as three commentaries on others' reports. The two sets of cases resemble each other closely in phenomenology and family history, dissolving, for the modern reader, the boundary between them and suggesting a severe mood disorder, most likely bipolar disorder.

De Clérambault conceived of erotomania as a syndrome of pathological emotions (*un syndrome passionnel morbide*) that followed an orderly evolution. The triad of hope, love, and

grandiosity (a translation of *orgueil* more in keeping with the sense of the text than "pride") was considered to be always present, with the last as the most important and, in fact, the "generator" of the syndrome. The "fundamental postulate" and the derivative theme that the object demonstrated a paradoxical or contradictory attitude toward the subject (evidence of the delusional nature of the beliefs) were the only ones that de Clérambault felt were constant, which was the misconception of Ellis and Mellsop (3). Since the evolution of affects follows a determined course, sudden onset was not a feature and does not serve as a point of comparison with Kraepelin's conception.

The thrust of the article, supported by the misapprehension of *orgueil* as pride, is to seek an explanation for erotomania and, by extension, the delusional (paranoid) disorders on psychodynamic grounds as the outcome of narcissistic injury—a view antithetical to that of both Kraepelin and de Clérambault. The poor review of the phenomenology of such a small portion of the cases in the English and French literature ignores the contribution of mood and organic disorders. Seeman's cases (4), used to defend that bias, actually support a division of patients into those with fixed beliefs (often not choosing a male of higher social status) who probably have schizophrenia or delusional disorders and those with recurrent delusions who suffer from a mood disorder, most likely bipolar disorder.

Rudden et al. (5) found erotically related beliefs, including sexual pursuit, in one-third of the women examined, along with significantly higher depression scores and more diagnoses of schizoaffective disorder or atypical psychosis. A second study (6) supported the association with bipolar disorder.

The article reiterates Kraepelin's views, which later, by their own pervasive influence on the authors of successive sets of criteria, found their way into the DSM-III-R definition of delusional (paranoid) disorders. It does not represent the views of de Clérambault or review the symptom or syndrome of erotomania.

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STEPHEN F. SIGNER, M.D.
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Dr. Segal Replies

SIR: Dr. Signer's letter illustrates some of the difficulties that may arise when one is discussing obscure, untranslated works, and though several of his points have merit, I do not believe that they seriously undermine my conclusions. For example, he suggests that the French word *orgueil* be translated as "grandiosity," which would be consistent with his own view of erotomanic delusions as largely symptoms of bipolar disorder.

der. I used the more traditional translation "pride." Shorter (1) has published (in French) one of the most detailed historical studies of de Clérambault's erotomania; he translates *orgueil* as "vanity," which is perhaps closer to my meaning than to Dr. Signer's. Shorter (personal communication) also supports my contention that de Clérambault saw emotional needs as shaping the *content* of the delusion, though not as its underlying cause. In fact, de Clérambault believed that all mental illness stemmed from physiological causes (in the case of the several different *psychoses passionnelles*, it was an ill-defined *automatisme mental*). My review should have made more explicit this distinction between theories of ultimate causality and theories that explain delusional content. It bears mentioning that today, 70 years after de Clérambault, we still can hardly go beyond saying that encapsulated delusional syndromes (delusional disorders in *DSM-III-R*) may have a physiological base (still unspecified and mysterious) and a psychologically meaningful content—perhaps, as I suggested, based on projection.

Dr. Signer is correct in stating that de Clérambault defined stages in the development of erotomania (as did Kraepelin). My remark about the sudden onset of the syndrome referred to the first, defining, delusional stage of the illness, the *stade d'espoir* (hopeful stage). My aim was to show that de Clérambault insisted that his "erotomania" differed from the paranoid erotic state described by Kraepelin (a distinction still made by French psychiatry), but that closer inspection fails to bear him out.

I agree with Dr. Signer that my review should have mentioned that erotomaniac delusions can occur in the context of affective or organic illnesses, as well as in schizophrenia and delusional disorder; the cases are more heterogeneous than has been thought. However, in the second study by Rudden et al. cited by Dr. Signer (which is the largest known collection of cases and which was published after my review), bipolar disorder finished a distant third (7% of cases) in the rank ordering of diagnoses for patients with erotomaniac delusions. Of the rest, 43% were schizophrenic, 25% had delusional disorder, erotomaniac type, and the remaining 25% were described as "other." True, many of these were apparently patients with schizoaffective disorder, but this diagnostic category may be more closely related to schizophrenia than has recently been thought (2). Nevertheless, Dr. Signer's point that erotomaniac delusions can occur in affective illness is well-taken. Although I mentioned several times that erotomaniac delusion may occur as a symptom of other illnesses, my review concerned primarily the "pure" form of the condition, now enshrined as delusional disorder, erotomaniac type. Dr. Signer's objections notwithstanding, I believe that the review is a useful summary and that its conclusions remain valid.

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JONATHAN H. SEGAL, M.D.
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Locked Seclusion for Children

SIR: We are writing in reference to the article "Is Locked Seclusion Necessary for Children Under the Age of 14?" by Terri Antoinette, R.N.C., and associates (1). In this study it

was found that rates of unlocked seclusion and medication administered as needed increased on three inpatient child psychiatry units following a state decree disallowing the use of locked seclusion. The authors concluded that "locked seclusion . . . should be considered a proper therapeutic intervention for severely disturbed youngsters."

This study is to be lauded for its attempts both to evaluate milieu interventions and to use empirical data to influence public policy. However, the article is more akin to a legal brief, arguing a specific position, than to an open-minded investigation. First, the literature review was significantly biased. While certainly not conclusive, several studies have suggested that seclusion is less effective than other management techniques (2, 3) and that the use of seclusion, as well as restraint, is determined as much by milieu factors as by patients' behavior (4-6). None of these studies was referenced in the article.

Second, the authors omitted one very important comparison in their data analysis. While they did briefly discuss the substantial differences in treatment response found in the three inpatient units, these differences should have been examined directly by including setting as an additional factor in the factor analyses. A significant main effect and a Seclusion by Setting interaction would have highlighted one of the study's most interesting results, i.e., that children in each of the units, which differed by age and diagnostic class, responded differently to both the cessation of locked seclusion and an alternative behavior management program. This differential response suggests either that patients of different ages and diagnoses respond differentially to the management techniques or that these techniques were applied inconsistently across the three units. The first possibility represents an interesting finding, for no study to date has directly examined subtypes of response to management techniques. The second possibility represents unwanted error.

Our final quarrel is with the use of the word "therapeutic" in the study's conclusion, a term usually used to refer to durable improvements in patients' conditions. In this case, therapeutic for whom? The staff or the patients? The study presents no direct data on patient behavior, only on staff response. Furthermore, Garrison et al. (5) found that there was no long-term decrease in problematic behavior following seclusion or restraint. We use seclusion and restraint, regularly and reluctantly, together with a systematic behavioral regimen on our inpatient child/adolescent unit. We do so primarily to ensure the patients' and staff's sense of personal safety, also ensuring a sense of order on the unit. However, neither the research by Ms. Antoinette and associates nor our own experience convinces us that seclusion and restraint are therapeutic in the conventional sense. As practitioners and researchers, we must avoid rationalization and be clear about both the reasons for our interventions and their expected outcomes.

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BRUCE ECKER, PH.D.
MATTHEW FRIEDMAN, M.D.
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SIR: The article by Ms. Antoinette and associates is a significant contribution to the debate about the use of seclusion on child and adolescent psychiatric inpatient services. It is unique to see a study begin research into the comparative use of limit-setting techniques: unlocked seclusion, behavioral-level systems, and use of medication as needed. This allows us to address questions such as, If we don't do something we think is countertherapeutic, what will we do instead? and Will the restrictive measure we adopt be more or less therapeutic than what we discarded? It also represents a creative use of data collected during a legislatively initiated period of restrictions on this intervention.

The article failed to review or reference the empirical literature on the use of seclusion with children and adolescents. For interested readers, I would like to include a selected list of references from the children's psychiatry literature (1-5) as an addendum to the excellent article. Much of this work has evolved out of papers, symposiums, workshops, and institutes sponsored by the American Academy of Child and Adolescent Psychiatry during its annual meetings. The academy members have taken a great interest in this area, and the academy's program committee has promoted research, discussion, and training in it. I personally have presented material on seclusion at these meetings since 1985. I also participate in the APA-sponsored course "Management of Difficult Children and Adolescents," directed by James C. McIntyre, M.D., which has been offered at several annual meetings.

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NANCY S. COTTON, PH.D.
Brookline, Mass.

Combat and Masculinity

SIR: A letter to the Editor from Dennis H. Grant, M.D. (1) says that men fighting in terrifying wars to prove maleness therewith develop posttraumatic stress disorder (PTSD). Not to worry! War is being desexed.

During the eons before the second half of this millennium's last century, warriors needed physical strength to hurl stones, wield massive swords, dig foxholes, throw up earthworks, or push cannon out of the mud. But no more. Today, devices applying electronics and internal combustion make aircraft, tanks, guided missiles, etc. operable by a light touch quite within most women's capacities. They break the link between combat and masculinity; they remove war from the roster of ways to prove masculinity.

So, in the next millennium, we will stop saying that a part of being male is to fight in a war, for it will be part of being female, too. Women will assume their half of the duty. Indeed, coed doubling of the pool from which combatants are drawn will halve a given man's risk of war-related PTSD.

But as long as survival constrains a group to compete for sustenance with other groups of its species, war will be practically inescapable.

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WILLIAM F. SHEELEY, M.D.
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Classification of Koro

SIR: In a recent article Ruth L. Bernstein, M.D., and Albert C. Gaw, M.D. (1) proposed a culture-specific classification of koro for *DSM-IV*. Several articles indicate an association of koro with panic disorder (2, 3). We present a case that questions the cultural specificity of fears of genital retraction and emphasizes the difficulty of designating these fears as a disorder rather than a symptom.

Mr. A, a 21-year-old Caucasian man, presented with a 6-month history of episodic tachycardia, tachypnea, chest pain, dizziness, diaphoresis, nausea, tinnitus, disturbance of spatial perception, difficulty concentrating, derealization, paresthesias, tremulousness, and fear of dying. These episodes occurred three to four times per day and lasted up to 30 minutes. He expressed extreme distress when he stayed alone, when driving, and when away from home. He also had a 1-month history of severe depressive symptoms. On the Structured Clinical Interview for *DSM-III* there was no indication of social or simple phobias, obsessive-compulsive disorder, or dysthymia. On the *SCL-90* he denied being bothered by sexual thoughts or thoughts of punishment for past sins, although he did express some feelings of guilt.

Mr. A had first experienced a spontaneous panic attack 6 years earlier. Further history revealed childhood separation anxieties and episodes in the seventh to ninth grades of paresthesias, feeling that his hair "stood on end" or that his head was "on fire," and seeing "stars and circles" when urinating. He saw a cardiologist, two family practitioners, and a urologist before seeing us. His diagnoses included mitral valve prolapse and "lazy eye" syndrome.

Eight days after beginning to take imipramine for panic disorder with agoraphobia and depression, Mr. A developed hesitancy on urination. He expressed concern about an old basketball accident in which he had fallen and struck his penis on a stone but had no apparent injury. By day 12 of treatment, he complained of moderate pain, hesitancy, and strain on urination. He then became increasingly anx-

ious and preoccupied with the fear that his penis was retracting. He had also had fears of genital retraction 6 years earlier when he used a vibrator two or three times for masturbation. He recalled panic-like symptoms when masturbating 3 or 4 years earlier and alluded to God's punishing him for his behavior. Decreases in his dose of imipramine reduced the urinary hesitancy and strain. Explanations about medication side effects and autonomic control of penile tumescence and size somewhat relieved his fears. However, the decreases in imipramine produced worsening of his panic attacks.

In this case, fear of genital retraction was not culture-bound. It did not occur in the context of an epidemic. The symptom was related to conditions that increase sympathetic tone, i.e., guilt and anxiety about sexual practices, penile manipulation, anticholinergic medication, and a predisposition to high-anxiety states. The findings in this case lead us to question whether Dr. Bernstein and Dr. Gaw's proposed classification scheme might be overly restrictive and, for some patients, genital retraction might be a multifactorial symptom rather than a specific disorder. This case emphasizes the need for careful elucidation of symptom sequence and patient psychodynamics in order to make the appropriate diagnosis.

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BARBARA KENNEDY, M.D., PH.D.
GENE R. FLICK, M.D.
Louisville, Ky.

SIR: I was delighted to read the article on koro and its proposed classification in *DSM-IV*. Besides being extremely informative, it gives us an opportunity to open a debate on this long-neglected but interesting syndrome.

There are, however, a few issues that I would like to bring up. There have been numerous cases of koro reported outside China and the Malay Archipelago, and perhaps the authors would agree with me that the syndrome has been underreported. I therefore feel that the syndrome cannot be called culture-bound or culture-specific. Its universal occurrence argues against any cultural constraints.

"Koro" is not a universal term even in areas where it is commonly found. The Chinese, for example, would not recognize it, as they use the term *soo-yang* instead. Indeed, the local beliefs about the causes of the syndrome and its management are quite different in China and the Malay Archipelago. Moreover, in China *soo-yang* was recorded as far back as 300 B.C., whereas in the Malay Archipelago koro is a relatively new illness. Thus, although the presentation of the syndrome is the same, the cultural beliefs about the disorder are quite different. In the West, a case of what appears to have been a koro-like syndrome was first described in the Middle Ages and attributed to witchcraft (1). This argues for a universality of the syndrome in its presentation but not in local beliefs. The

term "koro" has specific cultural connotations. The evidence shows that it is almost universal, although more prevalent in certain areas. I feel that the term "genital retraction syndrome," as suggested by Edwards (2), is a more appropriate term that reflects the universal nature of the disorder.

In the West, there are a few minor differences in the syndrome, in that the fear of death is less common. However, some patients have fears of changing sex or of a serious illness. The suggestion of Dr. Bernstein and Dr. Gaw that the diagnostic criteria should include a fear of impending death would be restrictive and ignore local beliefs.

In addition, I feel that it is misleading to state that the fear of genital retraction or death is primary, and anxiety is secondary. In most of the cases described in the Western literature, the patients have been under considerable stress and anxiety before developing the syndrome. The focus of anxiety is directed onto the genital area for various psychological or organic reasons, and this then predominates in the clinical presentation. Oyeboode et al. (3) were able to demonstrate exaggerated penile changes by making the subject think of the anxiety-provoking situation, thus giving an indication that anxiety may be the primary factor.

Most of the cases in the West are secondary to some other psychiatric disorder, but anxiety is present in all the cases. The syndrome usually responds to treatment of the primary disorder. I therefore feel that the axis I diagnosis should be that of the primary disorder, and the genital retraction syndrome should be a secondary diagnosis if the criteria are met. The criteria themselves need to be discussed and should take into account the universal nature of the disorder.

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DR. S.H.A. SAJJAD, M.R.C.PSYCH.
Carlow, Eire

SIR: The article on koro is important not only because it focuses attention on *DSM-IV* classification of the syndrome but also because it raises the general question of the position of culture-bound syndromes in *DSM-IV*. The authors propose that cases of koro may be diagnosed as 1) a physical condition, 2) a specific axis I disorder, 3) genital retraction disorder, culture-specific, and 4) genital retraction disorder, not culture-specific.

While koro presents heterogeneously, Dr. Bernstein and Dr. Gaw state that a central symptom is concern with genital retraction. We would point out that this symptom may fall within existing *DSM-III-R* categories, namely, body dysmorphic disorder or delusional disorder, somatic type, depending on whether or not it is of delusional intensity.

Dr. Bernstein and Dr. Gaw suggest that if a physical reason for the symptoms is found, a diagnosis of a physical condition is given. While this may be in line with the separation of delusional disorder, somatic type, from organic delusional disorder, current nosology may encompass both psychiatric and medical diagnoses. For example, if symptoms of obsessive-compulsive disorder develop following a viral encephalitis, both diagnoses are recorded.

The authors suggest that if the fear of genital retraction occurs in association with axis I symptoms, the diagnosis of the axis I disorder should be given. This is appropriate if the fear is preceded by or secondary to another axis I disorder. However, if the fear encompassed within body dysmorphic disorder or delusional disorder, somatic type, accompanies but is independent of another axis I disorder, both diagnoses may again be recorded. We are not certain that the separate classification of genital retraction syndrome, not culture-specific, is presently warranted. It appears that further research is required to establish the validity of this entity as distinct from body dysmorphic disorder, delusional disorder, somatic type, and obsessive-compulsive disorder.

Finally, Dr. Bernstein and Dr. Gaw suggest the diagnosis of genital retraction syndrome, culture-specific. While symptomatic belief in genital retraction may have different implications in different cultures, the label "culture-specific" may not be the optimal way of indicating this. Work on culture-bound syndromes highlights cultural factors in symptom production but also demonstrates that many, if not all, disorders are culture-bound (1). In particular, disorders involving concerns about the body, such as anorexia nervosa, may be seen as culture-bound (2). Labeling one disorder as culture-specific may therefore indicate cultural factors in its production, but it implicitly downplays cultural factors in other disorders.

The authors' work on koro makes an important contribution to the evolving conceptualization of the spectrum of body dysmorphic disorder (3). Conversely, the literature on body dysmorphic disorder and delusional disorder, somatic type, may be helpful to those interested in koro. The response of body dysmorphic disorder to serotonergic medications (4), for example, suggests that such medication may be useful in treating koro.

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Dr. Bernstein and Dr. Gaw Reply

SIR: The case reported by Dr. Kennedy and Dr. Flick is an interesting example of how the symptom of genital retraction can occur in another axis I disorder. In this case, panic disorder is the obvious diagnosis. If the symptom of genital retraction had been the chief complaint, then one might have considered the category of genital retraction disorder, not culture-specific, according to the scheme we proposed. This does not exclude a concurrent diagnosis of panic disorder.

We agree with Dr. Sajjad that the genital retraction complaint is universal. However, there are instances in which the form and presentation of the genital complaint, as in the case of koro and *suk-yeong*, are clearly conditioned by cultural beliefs and have resulted in an increased frequency of occur-

rence reaching even epidemic proportions. These are the cases we feel are specific to the culture in which they occurred and should be labeled differently. We suggest eliminating the indigenous, exotic names used to describe the phenomenon and replacing it with the descriptive term "genital retraction disorder," adding the subset "culture-specific" to show that some cases of the phenomenon are clearly more affected by culture than others.

We prefer the term "genital retraction disorder" rather than "genital retraction syndrome" because, as Dr. Sajjad suggests, it encompasses a variety of syndromes that differ in details. For example, many have argued for inclusion of the genital retraction disorder in the anxiety disorders. Certainly, anxiety is an important component. However, the somatic preoccupation is so dramatic and so affects the form of the disorder that to call it an anxiety disorder alone seems a little like putting the cart before the horse.

We seriously considered placing genital retraction disorder in the category of body dysmorphic disorder, a disorder characterized by preoccupation with some imagined defect in physical appearance in a normal-appearing person (*DSM-III-R*), as Dr. Stein and associates suggest. The reason we decided against this is that body dysmorphic disorder is a preoccupation with the appearance of a certain part of the body, as in someone who considers his nose too big. In contrast, those suffering from the genital retraction disorder are concerned with the active sag or dissolution of their genitals. We thought the difference between concerns over static appearance versus active transformation were significant enough to warrant a different category. In addition, there is usually a marked disruption of social and occupational functioning in cases of genital retraction disorder because of concurrent panic or anxiety, which is not commonly present in body dysmorphic disorder.

Delusional disorder, somatic type, should be part of the differential diagnosis. However, we stress the point that most cases of genital retraction are not delusional per se; the patients experience actual mild shrinkage associated with anxiety (1) and, generally speaking, their ego functions are intact. This is particularly the case among individuals from a culture where genital retraction disorder is seen as a significant danger.

REFERENCE

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RUTH L. BERNSTEIN, M.D.
ALBERT C. GAW, M.D.
Boston, Mass.

Comments on Report on *DSM-IV*

SIR: Having recently been appointed as advisor to the Dissociative Disorders Work Group of the Task Force on *DSM-IV* to examine childhood dissociative disorders (1), I was excited to see the article "DSM-IV: Work in Progress" (2). My excitement faded when I realized that the work group and its chairman, David Spiegel, M.D., were not mentioned. Was this an oversight, or has there been no progress to report in dissociative disorders?

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2. Frances A, Pincus HA, Widiger TA, Davis WW, First MB: *DSM-IV: work in progress*. *Am J Psychiatry* 1990; 147: 1439-1448

GARY PETERSON, M.D.
Chapel Hill, N.C.

SIR: In their comprehensive article "*DSM-IV: Work in Progress*," Dr. Frances and associates indicate their concern regarding possible abuses of the *DSMs*, including "the assessment of criminal responsibility, in which the presence of a diagnosable *DSM* disorder should not be regarded as sufficient to confer the sick role." They further state that it is "often the case" that "the presence of a *DSM* diagnosis . . . [is] important in reimbursement and disability decisions."

Regarding the former concern, I am sorry to find this prejudice offhandedly expounded by experts in psychiatric diagnosis. Again, someone is afraid that some guilty person will "get off" because of psychiatric involvement. Putting aside the infinitesimal percentage of insanity defenses (especially, successful insanity defenses) and putting aside the fact that the jails are filling up with seriously mentally ill defendants as both civil treatment and criminal justice diversions vanish, the problem the authors pose is dealt with in the law and definitions of criminal capacity or responsibility, since such issues are a matter of specific *functional* capacity or ability, not diagnosis. No individual is "not guilty by reason of schizophrenia" or "incompetent by reason of major depression." Defendants are "insane" or "incapable" because they possessed or did not possess certain specific states of mind. The problem lies, rather, in the criminal justice system, which often disallows or devalues an impairment unless it fits perfectly within a *DSM* label.

Regarding the latter issue, use and misuse of *DSM* labels in disability determinations is not merely possible; in some jurisdictions their use is required by law. The following is from the "cleanup legislation" to implement new California workers' compensation "reforms":

Psychiatric injuries must be diagnosed according to terminology and criteria of [sic] American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Third Edition-Revised (*DSM-III-R*), pending promulgation of procedures by the Industrial Medical Council.

As promulgators and purveyors of the *DSMs*, we and our organization must exert some controls over their use and misuse. I am a forensic psychiatrist, active in the criminal, civil, and workers' compensation areas. I know the problem is very serious. It hurts doctors and it hurts patients. Perhaps consideration should be given not only to educating the nonpsychiatric professionals (primarily legal and legislative) who are misusing the *DSM* diagnoses but also to requiring our members to act affirmatively whenever they encounter these abuses.

MICHAEL B. COBURN, M.D.
Van Nuys, Calif.

SIR: In their article Dr. Frances and associates provided an informative overview of their work on *DSM-IV* and graciously invited readers' comments. Some of my questions on *DSM-III-R* follow.

1. In contrast to other diagnostic systems, *DSM-III-R* does not require a minimum duration of disturbance to make the diagnosis of manic or hypomanic syndrome. Does this not

create a definitional boundary problem? For while the boundary between manic and hypomanic is defined by level of impairment, there is no defined way to differentiate between hypomanic and normal. This is more than a semantic quibble, since the diagnosis and differential treatment of bipolar disorder not otherwise specified (which includes bipolar type II) or cyclothymia, in contradistinction to the unipolar disorders, may depend on the presence of an operationally defined hypomanic episode.

2. *DSM-III-R* states that major depression is subclassified as recurrent if there are two or more episodes separated by a period of 2 months of usual functioning. It further states that the later episode need not meet full criteria for a major depressive episode if there has been a previous major depressive episode.

This raises two problems. First, requiring only 2 months of wellness following a depressive episode fails to distinguish between the concepts of relapse and recurrence. The predominant trend in the recent literature (1, 2) appears to view the reemergence of symptoms as a relapse of the previous depressive episode if it occurs within as much as 6 months—but surely not merely 2 months—of that episode. The clinical ramifications include issues of prognosis and treatment. For example, some pharmacologic agents appear effective in preventing relapse but not recurrence (1, 2).

With respect to *DSM-III-R* not requiring full criteria for the second episode, this appears to diminish greatly the reliability of the diagnostic label of recurrence and obfuscates the applicability of the results of the relevant longitudinal research studies.

3. Can't the definition of schizoaffective disorder be greatly simplified by requiring merely the presence of psychosis (delusions or hallucinations) during a period of mood disturbance, rather than the cumbersome *DSM-III-R* requirement for the presence of the cross-referenced "A criterion of Schizophrenia"? This proposed simplification would seem to add to the usefulness of this diagnostic category without sacrificing its validity.

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1. Montgomery SA, Dufour H, Brion S, Gailledreau J, Laqueille X, Ferrey G, Moron P, Parant-Lucena N, Singer L, Danion JM, et al: The prophylactic efficacy of fluoxetine in unipolar depression. *Br J Psychiatry* 1988; 153(suppl 3):69-76
2. Georgotas A, McCue RE, Cooper TB: A placebo-controlled comparison of nortriptyline and phenelzine in maintenance therapy of elderly depressed patients. *Arch Gen Psychiatry* 1989; 46:783-786

BRIAN LADDS, M.D.
New York, N.Y.

Dr. Frances and Associates Reply

SIR: Dr. Peterson, Dr. Coburn, and Dr. Ladds have made a number of very important observations. We can only respond telegraphically here, but we will be addressing most of these issues in more detail in the *DSM-IV Options Book*, which will be published this fall.

We are sorry to have disappointed Dr. Peterson by not including information on dissociative disorders in our article. This was neither an oversight nor an indication of lack of progress but, rather, a consequence of tight space constraints. Indeed, Dr. Spiegel and the group working on dissociative disorders have made a great deal of progress, which will be re-

flected in the *Options Book*. They have written a series of informative literature reviews on the various dissociative disorders and are now conducting a MacArthur Foundation-funded reanalysis of data on brief reactive dissociative disorders and acute stress disorder (a newly proposed category).

We agree strongly with Dr. Coburn's concern about the use and misuse of *DSM-IV* diagnoses in forensic, reimbursement, and disability determinations. It is our intention in developing *DSM-IV* to be sensitive to these issues and to try to make it more difficult for such misuses to take place. We intend to address this problem in the introductory chapter of *DSM-IV* through a somewhat expanded discussion of the appropriate use of psychiatric diagnoses in such determinations. In addition, APA's Task Force on the Use and Misuse of Psychiatric Diagnoses in the Courts is in the process of preparing a report that should be quite helpful, and this will be referenced in *DSM-IV*.

The boundary between manic and hypomanic episodes and normal elevated mood is important to establish and, as pointed out by Dr. Ladds, pertains directly to the issue of "bipolar II." After a literature review in this area, we have begun a seven-site international data reanalysis project funded by the MacArthur Foundation that will include information on several hundred "bipolar II" patients. This should help us in deciding whether to include a specific category for bipolar II in *DSM-IV*, and if so, how best to define a hypomanic episode and the number of hypomanic episodes that would be required.

Dr. Ladds also raises important points regarding the interval required for establishing recurrence in recurrent major depression and also whether to allow the counting of the second or later episode(s) when the full criteria are not met. Both points are receiving careful consideration. The major reason *DSM-III-R* did not require meeting the full syndromal criteria for later episodes of recurrent depression was to allow early diagnosis and treatment of a given episode when this seemed reasonable in the context of a recurrent disorder. However, this exception does create problems of its own and may be dropped in *DSM-IV*.

Dr. Ladds's suggestion in regard to the definition of schizoaffective disorder has the advantage of simplifying the criteria, but it would also have the effect of broadening the construct and changing the definition of "caseness." We may not have sufficient empirical data to determine whether such changes are warranted.

We are grateful for the thoughtful comments of our correspondents.

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Reprints of letters to the Editor are not available.

Corrections

In the article "Parents' Emotional Neglect and Overprotection According to the Recollections of Patients With Borderline Personality Disorder" by Hallie Zweig-Frank, Ph.D., and Joel Paris, M.D. (May 1991 issue, pp. 648-651, two numbers in table 1 were reversed: for hospitalized female borderline patients, the SD for mother protection should be 10.0, and the mean for father protection should be 16.9.

In the article "Nicotine Potentiation of Haloperidol in Reducing Tic Frequency in Tourette's Disorder" by Brian J. McConville, M.D., et al. (June 1991 issue, pp. 793-794), there was an error in the grant support acknowledgment. The correct name for the third group is The Smokeless Tobacco Research Council, Inc.

Highlights of the 144th Annual Meeting

The 144th Annual Meeting of the American Psychiatric Association was held in New Orleans, Louisiana, May 11–16, 1991. The total registration was 13,466, including 6,820 members; 1,977 spouses, other family members, and guests; 3,166 nonmembers; 1,211 exhibitors; 107 members of the media; and 185 staff members.

Opening Session

The opening session was called to order by Elissa P. Benedek, M.D., 119th President of the Association, on Sunday evening, May 12 in the New Orleans Hilton. Dr. Benedek introduced The Honorable Lindy Boggs who offered official greetings to the membership from the city of New Orleans.

Dr. Benedek then announced the winners of the APA poster contest. The winners and their parents were: *Kindergarten*—First Place: Pooja Pandya, Parent: Asha Pandya, M.D.; Second Place: Gabriel Saenz, Parent: Irene E. Ortiz, M.D.; Third Place: Krystyna Wamboldt, Parent: Marianne Wamboldt, M.D.; *First Grade*—Tied for First Place: Erin Kravitz, Parent: Kerry D. Kravitz, M.D., and Alexander Leigh, Parent: Hoyle Leigh, M.D.; Second Place: Gabriel Smedresman, Parent: Devra Braun, M.D.; Third Place: Nicole Luna, Parent: Roberto Luna, M.D.; *Second & Third Grades*—Tied for First Place: Tristan Noone, Parent: Joe A. Noone, M.D., and Sat Shenoy, Parent: Chitra Shenoy, M.D.; Second Place: Jesse Geller, Parent: Jeffrey L. Geller, M.D.; Tied for Third Place: Jonathan Betts Fields, Parent: Dexter L. Fields, M.D., and Van Elliott Griffith, Parent: James L. Griffith, M.D.; *Fourth & Fifth Grades*—First Place: Maya Gideon, Parent: Ruth Gandell Gideon, M.D.; Second Place: Karen Harichandran, Parent: Dharmini Harichandran, M.D.; Third Place: Dexter Fields, Parent: Dexter L. Fields, M.D.; *Sixth–Ninth Grades*—First Place: Rivi Handler-Spitz, Parent: Harlan Spitz, M.D.; Second Place: Marianna Louise Griffith, Parent: James L. Griffith, M.D.; Third Place: Sharon Harichandran, Parent: Dharmini Harichandran, M.D.; *Honorable Mention for the youngest participant*: Bill Menninger Johnson, Parent: Eliza Menninger, M.D.

Dr. Benedek introduced those seated on the stage with her: the members of the APA Board of Trustees, officers of the APA Assembly, and Past Presidents of the Association. Dr. Benedek then recognized members of the audience, including the members of the Assembly Executive Committee; Past Speakers of the Assembly; Past Vice-Presidents of the Association; newly elected national officers, trustees, and Assembly officers; presidents of APA district branches; chairpersons of APA councils, commissions and joint commissions; and the APA Medical Director. She then thanked the members of the Assembly for their hard work and dedication.

Allan Tasman, M.D., chairperson of the Scientific Program Committee, and Daniel K. Winstead, M.D., chairperson of the Local Arrangements Committee, were introduced and thanked by Dr. Benedek; each then presented brief reports.

Dr. Benedek then thanked and recognized the following distinguished representatives of psychiatric and other related organizations from the United States and abroad:

Representatives of Organizations in the United States: George H. Allison, M.D., President, American Psychoanalytic Association; Kenneth Z. Altshuler, M.D., President, American Association of Chairmen of Departments of Psychiatry; Glen F. Aukerman, M.D., Presi-

dent, American Academy of Family Physicians; Sheila G. Baler, Ph.D., President, American College of Mental Health Administration; Allan Beigel, M.D., President, Group for the Advancement of Psychiatry; William E. Bell, M.D., President, American Board of Psychiatry and Neurology, Inc.; Samuel Bravo-Williams, M.D., President, International Association of Gerontology; Robert H. Bruininks, M.D., President, American Association on Mental Retardation; Thomas K. Ciesla, M.D., President, National Guild of Catholic Psychiatrists; Rabbi Jeffrey Cohen, D.Min., President, Association of Mental Health Clergy; Suzanne Dandoy, M.D., President, American College of Preventive Medicine; Robert B. Daroff, M.D., President, American Neurological Association; Nicholas E. Davies, M.D., President, American College of Physicians; Prakash Desai, M.D., President, National Association of VA Chiefs of Psychiatry; K. Himasiri De Silva, M.D., President, Sri Lankan Psychiatrists in America; Darryl C. DeVivo, M.D., President, Child Neurology Society; Bernard M. Dickens, LL.D., Ph.D., President, American Society of Law and Medicine; Leah J. Dickstein, M.D., President, Association of Women Psychiatrists; Paul Dorfner, M.S., President, National Mental Health Consumers Association; Antoinette Parisi Eaton, M.D., President, American Academy of Pediatrics; Richard L. Edwards, Ph.D., President, National Association of Social Workers, Inc.; Roselyn Payne Epps, M.D., President, American Medical Women's Association, Inc.; Paul Errera, M.D., Director, Mental Health & Behavioral Sciences Service, Department of Veterans Affairs; Merli G. Fermo, M.D., President, Philippine Psychiatrists of America; Desmond S. Fung, M.D., President, Association of Chinese American Psychiatrists; Seymour Gers, M.D., President, American Society of Psychoanalytic Physicians; Elliot S. Gershon, M.D., President, American Psychopathological Association; James O. Gibson, President, Association of Mental Health Administrators; Gary Goldsmith, President, National Depressive and Manic-Depressive Association; Richard L. Goode, M.D., President, American Academy of Otolaryngology—Head & Neck Surgery; Frederick K. Goodwin, M.D., Administrator, Alcohol, Drug Abuse and Mental Health Administration; Enoch Gordis, M.D., Director, National Institute on Alcohol Abuse and Alcoholism; John F. Greden, M.D., President, Society of Biological Psychiatry; Robert E. Hales, M.D., President, Association for Academic Psychiatry; James A. Hawkins, B.A., President, American Mental Health Fund; Leslie Herz, Ed.M., President, American Psychiatric Association Auxiliary; Harvey A. Horowitz, M.D., President, American Society for Adolescent Psychiatry; Neil J. Jacobson, Ph.D., President, Association for the Advancement of Behavior Therapy; Lucille A. Joel, Ed.D., R.N., President, American Nurses Association; Charles Johnson, M.D., President, National Medical Association; John C. Johnson, M.D., President, American College of Emergency Physicians; Edward R. Kaufman, M.D., President, The American Academy of Psychiatrists in Alcoholism and Addictions; Witold Kawecki, M.D., President, Association of Polish Psychiatrists and Neurologists in America; Stanley R. Kern, M.D., President, American Board of Forensic Psychiatry, Inc.; Haydee C. Kort, M.D., President, American Association of Psychiatric Administrators; Maurice Leduc, M.D., President, Canadian Psychoanalytic Society; Robert L. Leon, M.D., President, American Association for Social Psychiatry; Alan I. Leshner, Ph.D., Acting Director, National Institute of Mental Health; Bennett Leventhal, M.D., President, Society of Professors of Child and Adolescent Psychiatry; Theodore Lidz,

M.D., President, American College of Psychoanalysts; Constance E. Lieber, B.A., President, National Alliance for Research on Schizophrenia and Depression; Jonathan D. Lieff, M.D., President, American Association for Geriatric Psychiatry; Don R. Lipsitt, M.D., President, American Association of General Hospital Psychiatrists; Sidney Malitz, M.D., President, Benjamin Rush Society; Velandy Manohar, M.D., President, American Association of Psychiatrists from India; James L. McGaugh, Ph.D., President, American Psychological Society; Robert M. Morse, M.D., President, Association for Medical Education and Research in Substance Abuse; Eli Newberger, M.D., President, American Orthopsychiatric Association; Russell Noyes, Jr., M.D., President, Academy of Psychosomatic Medicine; Werner J. Pankratz, M.D., President, Canadian Psychiatric Association; Thomas M. Posey, M.S., President, National Alliance for the Mentally Ill; Ghulam Qadir, M.D., President, Pakistan Psychiatric Society of America; Richard T. Rada, M.D., President, American Academy of Psychiatry and the Law; Anthony B. Radcliffe, M.D., President, American Society of Addiction Medicine; Frederick D. Raine, M.B.A., President, National Association of Private Psychiatric Hospitals; Thomas R. Reardon, M.D., Member, Board of Trustees, American Medical Association; Peter F. Regan, M.D., President, The American College of Psychiatrists; Thomas D. Romeo, M.S.W., President, National Association of State Mental Health Program Directors; Roger N. Rosenberg, M.D., President, American Academy of Neurology; Deborah C. Roth, D.O., President, Association of Directors of Medical Student Education in Psychiatry; Elisabeth Rukeyser, Chairman of the Board, National Mental Health Association; Joseph Sapira, M.D., President, American Psychosomatic Society, Inc.; John E. Schowalter, M.D., President, American Academy of Child and Adolescent Psychiatry; Alvin L. Schultz, M.D., President, Council of Medical Specialty Societies; Charles R. Schuster, Ph.D., Director, National Institute on Drug Abuse; Richard H. Schwarz, M.D., President, American College of Obstetricians and Gynecologists; M. Ali Shamie, M.D., President, Society of Iranian Psychiatrists in North America; George M. Simpson, M.D., President, American College of Neuropsychopharmacology; Isaac Slaughter, M.D., President, Black Psychiatrists of America; James B. Smith, M.D., President, American Academy of Clinical Psychiatrists; Steven J. Solomon, Ph.D., President, National Council of Community Mental Health Centers; Frank C. Spencer, M.D., President, American College of Surgeons; Charles D. Spielberger, Ph.D., President, American Psychological Association; Walter N. Stone, M.D., President, American Group Psychotherapy Association; Mahmoud S. Taman, M.D., President, Arab American Psychiatrists Association of America; Clifton R. Tennison, Jr., M.D., President, American Association of Community Psychiatrists; Jaime Trujillo, M.D., President, American Society of Hispanic Psychiatrists; Ulku Ulgur, M.D., President, Turkish-American Neuropsychiatric Association; Josef H. Weissberg, M.D., President, American Academy of Psychoanalysis; Sidney H. Weissman, M.D., President, American Association of Directors of Psychiatric Residency Training, Inc.

International Scholars: Ambassador Tahseen Basheer, former Egyptian Ambassador to Canada; Prof. Mingdao Zhang, Vice-Director, Shanghai Institute of Mental Health; Dr. Semyon F. Gluzman, Soviet psychiatrist; Prof. Juan Ramon de la Fuente, M.D., Dean of Faculty of Medicine at the National University of Mexico; Daniel N. Stern, M.D., Professor of Psychology at the University of Geneva in Switzerland.

Representatives of Other International Organizations and Psychiatric Associations in Other Countries: Prof. Peter Berner, Austrian Association of Neurology and Psychiatry; Dr. Roger Montenegro, Association of Argentine Psychiatrists; Dr. Gordon Parker, Royal Australian and New Zealand College of Psychiatrists; Dr. M. Van Mofaert, Flemish Association of Psychiatry and Neurology; Dr. Rodolfo Fahrner, Argentine Society of Consultation-Liaison Psychiatry and the InterAmerican Council of Psychiatric Organizations; Dr. Othon Bastos, Brazilian Psychiatric Association; Dr. Petko Dontchev, Bulgarian Psychiatric Association; Dr. Otto Doerr, Chilean Society of Psychiatry and Neurology; Dr. Roberto Chaskel, Colombian Psychiatric Association; Prof. Petr Zvolsky, Czechoslovak Psychiatric Association; Dr. Anne Lindhardt, Danish Psychiatric Society; Dr. Carlos Leon-Andrade, Ecuadorian Psychiatric Association; Dr. Simon-Daniel Kipman, Association Francaise de Psychiatrie; Prof. Uwe Peters, German Society for Psychiatry and Nervous Diseases; Dr. Augusto Aguilera,

Psychiatric Association of Guatemala; Dr. Bela Buda, Hungarian Psychiatric Association; Dr. Art O'Connor, Irish Division of the Royal College of Psychiatrists; Dr. Tomas Zoega, Icelandic Psychiatric Association; Prof. Piero Sarteschi, Italian Society of Psychiatrists; Dr. Satoshi Shikiba, Japanese Association of Psychiatric Hospitals; Prof. Chung Kyoan Lee, Korean Society of Biological Psychiatry; Prof. Andrew Sims, Royal College of Psychiatrists of Great Britain; Dr. Lauro Castaneda de Alba, Mexican Psychiatric Association; Prof. F. G. Zitman, Netherlands Psychiatric Association; Prof. Per Vaglum, Nordic Psychiatric Associations; Prof. O.W. Steinfeldt-Foss, Norwegian Psychiatric Association; Prof. Jacek Bomba, Polish Psychiatric Association; Prof. Jose D. Cordeiro, Association of Portuguese Psychiatry; Dr. George Hart, Society of Psychiatrists of South Africa; Dr. Vanpen Boonyaprakob, Psychiatric Association of Thailand; Dr. Wei-Tsuen Soong, Society of Psychiatry of the Republic of China (Taiwan); Prof. Enrique Probst, Society of Psychiatry of Uruguay; Dr. Antonio Pacheco Hernandez, Venezuelan Psychiatric Association; Dr. Ruben Hernandez-Serrano, Venezuelan Medical Federation; Dr. Irving Philips, International Association on Child and Adolescent Psychiatry and Allied Professions; Prof. R. Volmat, International Society of Art and Psychopathology; Dr. Gaston P. Harnois, World Association for Psychosocial Rehabilitation; Dr. Gamal M. Abou El Azayem, World Federation for Mental Health; Dr. Jorge Alberto Costa e Silva, World Psychiatric Association.

George Tarjan, M.D., introduced Dr. Benedek, who gave the Presidential Address, "Looking Ahead: New Psychiatry, Old Values" (printed elsewhere in this issue of the *Journal*). Paul J. Fink, M.D., introduced Lawrence Hartmann, M.D., President-Elect of the Association, who gave the Response to the Presidential Address, "Humane Values and Biopsychosocial Integration" (printed elsewhere in this issue). Dr. Benedek then adjourned the opening session.

Business Meeting

The Annual Business Meeting was called to order by Elissa P. Benedek, M.D., in the New Orleans Convention Center on Monday, May 13, at 12:30 p.m.

First session. Ronald A. Shellow, M.D., Recorder, called the roll of the Assembly representatives and announced the presence of a quorum. Dr. Irvin M. Cohen, Past Speaker, spoke in tribute to Hamilton F. Ford, M.D. (1908–1990)—Speaker 1966–1967. Dr. Donald G. Langsley, Past President, then spoke in tribute to C.H. Hardin Branch, M.D. (1908–1990)—President 1962–1963. Dr. Benedek then asked the audience to observe a moment of silence in memory of all members and Fellows who died during the past year. Richard Goldberg, M.D., member of the Committee of Tellers, announced the results of the election of officers and trustees. The reports to the membership followed. Philip M. Margolis, M.D., presented the Secretary's report, which was followed by the reports of Mary Jane R. England, M.D., Treasurer; Edward Hanin, M.D., Speaker of the Assembly; G. Thomas Pfahler, M.D., Speaker-Elect of the Assembly; William B. Spriegel, M.D., chairperson of the Committee on the Constitution and By-Laws; and Donna M. Norris, M.D., chairperson of the Membership Committee. Melvin Sabshin, M.D., presented the Medical Director's report. Reports of all the councils were also available. All reports were accepted by the membership as submitted and will be published in the October 1991 issue of the *American Journal of Psychiatry*.

Dr. Harvey Bluestone presented the Speaker's plaque to Edward Hanin, M.D., retiring Speaker, and Dr. John S. McIntyre presented the Vice-President's badge to Fred Gottlieb, M.D., retiring Vice-President. Dr. Carol C. Nadelson presented the President's badge to Dr. Benedek. Dr. Benedek then recessed the first session of the business meeting.

Second Session. Following the business meeting Dr. Benedek called the Annual Forum, for all voting members, to order. Dr. Lester Shapiro spoke again this year of his concerns regarding industry sponsored symposia. He proposed that a task force be established to look into the implications of these symposia. This motion was debated on the floor and then defeated.

A member from California addressed the gathered members regarding anti-psychiatry groups and asked for adoption of a resolution. Dr. Benedek assured the gathered members that this issue was already

under consideration and would be addressed at future Board of Trustees meetings, including the June 1991 Board meeting.

Dr. Michael Cleary, a member from Arizona, rose and spoke of the APA's activities regarding abortion. He was concerned that the APA not take an "activist" role on this issue. Dr. Benedek assured Dr. Cleary that the Association has a long-held position on abortion and that it is the role of the President and the other officers to support the Association's official, well-thought out positions as they carry out their duties. She also noted that she respects and welcomes polite disagreement.

The Annual Business Meeting and Forum were adjourned by Dr. Benedek at 2:10 p.m.

Convocation

The 35th Convocation of Fellows was held in the New Orleans Hilton beginning at 8:30 p.m. on Monday, May 13. Dr. Benedek presided. After the processional march, Dr. Benedek called the Convocation to order. Dr. Benedek thanked Dr. Edward A. Siegel of San Diego, California, for playing the music during the processional. The Reverend Prim Smith, Chaplain at Tulane University School of Medicine, gave the invocation. President-Elect, Lawrence Hartmann, M.D., then led the ceremony conferring Life Fellowship and the induction of Fellows of the Association. Dr. Benedek read the names of the 1990 Corresponding Fellows: Osama Mohd Al-Radi, M.D., Taif, Saudi Arabia; Ashish K. Basu, M.D., Calcutta, India; Marc Louis Bourgeois, M.D., Bordeaux, France; Miguel Roberto Jorge, M.D., Sao Paulo, Brazil; Amelia E. Musacchio de Zan, M.D., Buenos Aires, Argentina; Eugene Stern Paykel, M.D., Cambridge, England; Yu-cun Shen, M.D., Beijing, People's Republic of China.

The following 50-Year Life Fellows and Life Members (1941-1991) were then recognized: John A. Aita, M.D., Omaha, NE; Robert C. Anderson, M.D., Covington, GA; Frances Arkin, M.D., Miami Beach, FL; Jacob A. Arlow, M.D., New York, NY; Charles C. Ault, M.D., Sherwood, AR; Alfred P. Bay, M.D., Carthage, MO; Louis Belinson, M.D., Largo, FL; H. Craig Bell, M.D., Abington, PA; Sophie Bookhalter, M.D., New York, NY; Charles Brenner, M.D., New York, NY; Willard C. Brinegar, M.D., Norfolk, NE; Matthew Brody, M.D., Brooklyn, NY; Meyer Brown, M.D., Wilmette, IL; Albert N. Browne-Mayers, M.D., Willimantic, CT; Rex E. Buxton, M.D., Bethesda, MD; Dale C. Cameron, M.D., San Diego, CA; Paul T. Cash, M.D., Des Moines, IA; Carmelo J. Chiarello, M.D., Shirley, NY; Dominick F. Chirico, M.D., Little Neck, NY; Robert A. Cohen, M.D., Bethesda, MD; George M. Cowan, M.D., Duluth, MN; H. Harlan Crank, M.D., Austin, TX; Harry C. Dunstone, M.D., Angel Fire, NM; Marianne H. Eckardt, M.D., New York, NY; William S. Fife, M.D., Orangevale, CA; Sydney G. Fine, M.D., Titusville, NJ; Elizabeth D. Fletcher, M.D., Little Rock, AR; David J. Flicker, M.D., South Orange, NJ; William Furst, M.D., West Orange, NJ; Phillip H. Gates, M.D., Lexington, MA; Alexander Gralnick, M.D., Port Chester, NY; Eugene W. Green, M.D., Columbus, OH; William F. Green, M.D., San Diego, CA; Bernard L. Greene, M.D., Murieta Hot Springs, CA; Alexander Halperin, M.D., Washington, DC; Max Hayman, M.D., Rancho Mirage, CA; Philip H. Heersema, M.D., San Francisco, CA; Carl H. Jonas, M.D., Belmont, CA; Lothar B. Kalinowsky, M.D., New York, NY; Mark Kanzer, M.D., Harrison, NY; Emma M. Kent, M.D., Lakewood, CO; Richard H. Lambert, M.D., Santa Barbara, CA; Paul V. Lemkau, M.D., Lusby, MD; Erwin Levy, M.D., New York, NY; Louis Linn, M.D., New York, NY; Milton Lozoff, M.D., San Mateo, CA; Harry L. Mackinnon, M.D., Naples, FL; Burdett H. McNeel, M.D., Scarborough, ON, Canada; Leslie A. Osborn, M.D., Scottsdale, AZ; Bernard L. Pacella, M.D., New York, NY; Samuel Paster, M.D., Santa Monica, CA; Isidore Portnoy, M.D., New York, NY; Edward A. Posell, M.D., Sunnyvale, CA; Ian Paley Rak, M.D., Sandwich, MA; James E. Rappa, M.D., New Paltz, NY; Gregory Rochlin, M.D., Cambridge, MA; John R. Saunders, M.D., Richmond, VA; Lazarus Secunda, M.D., Medfield, MA; Norman R. Shulack, M.D., South Miami, FL; I. Ronald Sonenthal, M.D., Houston, TX; Isadore Spark, M.D., Willow Grove, PA; Leo A. Spiegel, M.D., New York, NY; Hyman Spotnitz, M.D., New York, NY; Maurice D. Spottswood, M.D., Napa, CA; Theodore P. Suratt, M.D., Cleveland Heights, OH; Sidney L. Tamarin, M.D., Ithaca, NY; Edward S. Tauber, M.D., E. Greenwich, RI; David Tillim, M.D., Bronx, NY; George J. Train, M.D., New

York, NY; Steven L. Van Riper, M.D., Detroit, MI; William Weisdorf, M.D., Glencoe, IL; William Winick, M.D., Brockton, MA; Isidore Ziferstein, M.D., Ph.D., Los Angeles, CA; Eugene Ziskind, M.D., Los Angeles, CA. Dr. Benedek then presented Honorary Fellows, Dr. Ellen Frank and Dr. Myrna M. Weissman, and Distinguished Fellow, Dr. Norman Sartorius, with their medallions and certificates.

Special Presidential Commendations were presented to Colonel Joe G. Fagan, M.D., "in recognition of his exceptional efforts to provide high quality psychiatric care, as well as psychiatric education for the military"; to JoAnn E. Macbeth, J.D., "in recognition of her outstanding grasp of ethical issues and their relationship to psychiatric practice"; to Carol C. Nadelson, M.D., "in recognition of her devotion, energy, skill and effectiveness as Editor-in-Chief of American Psychiatric Press, Inc."; to Loren H. Roth, M.D., "in recognition of his untiring efforts to improve the human rights and eliminate psychiatric abuse of patients in the Soviet Union"; to Congresswoman Patricia Schroeder, "in recognition of her untiring efforts to improve the health and mental health care of women and families in the United States"; to George Tarjan, M.D., "in recognition of his outstanding leadership in the field of child psychiatry, especially with the mentally retarded"; and to Raymond W. Waggoner, Sr., M.D., "in recognition of his unfailing devotion to the current issues confronting American psychiatry, and his ability to use insights gained from a long career in psychiatry and apply them to today's problems."

Dr. Benedek introduced Faye Wattleton, President of Planned Parenthood Federation of America, Inc. Ms. Wattleton gave the William C. Menninger Memorial Convocation Lecture, "Every Child a Wanted Child: Reproductive Rights and the Future of America."

After introducing the chairpersons of the award committees, Dr. Benedek presented the 1991 awards. Distinguished Service Awards were presented to David A. Hamburg, M.D., President of the Carnegie Corporation of New York; and to Carolyn B. Robinowitz, M.D., Senior Deputy Medical Director of the APA; and the Institutional Distinguished Service Award was presented to the Alcohol, Drug Abuse, and Mental Health Administration, and was accepted by Frederick K. Goodwin, M.D., Administrator, ADAMHA. This award was established by the Board of Trustees in 1964 to honor APA members who have contributed exceptional meritorious service to American psychiatry, and to groups which have benefitted the APA, the field of psychiatry, or the mentally ill.

Jack F. Wilder, M.D., Professor of Psychiatry and Director of the Mental Health Education Program at the Albert Einstein College of Medicine at Yeshiva University in the Bronx, New York, received the Administrative Psychiatry Award. Established in 1983, this award honors an APA member who is a nationally recognized clinician executive, whose effectiveness as an administrator of major mental health programs has expanded the body of knowledge of management in the mental health services delivery system, and whose effectiveness has made it possible for them to function as a role model for other psychiatrists.

The APA/Dista Products Resident Research Award, established in 1985 to honor a psychiatry resident for excellence in research undertaken during residency, was presented to Gianni L. Faedda, M.D., a psychiatry resident at McLean Hospital in Belmont, MA; to Eric A. Nofzinger, M.D., a psychiatry resident at Western Psychiatric Institute and Clinic in Pittsburgh, PA; to Katharine A. Phillips, M.D., a psychiatry resident at McLean Hospital in Belmont, MA; and to Andrew J. Stoll, M.D., also a psychiatry resident at McLean Hospital in Belmont, MA.

The APA/Wisniewski Young Psychiatrist Research Award, established in 1990 in honor of the late Dr. Alexander A. Wisniewski to recognize significant research accomplishments or promise of young psychiatrists, was presented to Stephen G. Rayport, M.D., Assistant Professor of Clinical Psychiatry at Columbia University and a research psychiatrist at New York State Psychiatric Institute.

The Marie H. Eldredge Award, established in 1964 to honor an APA member or resident residing and working in Hawaii, Pennsylvania, or New Jersey, and recognizing research work into the cause and treatment of neuroses and retardation, was presented to Marilyn Wright, M.D., Department of Psychiatry, University of Hawaii.

The Foundations' Fund Prize for Research in Psychiatry, established to recognize outstanding research in psychiatry and its basic

sciences, was awarded to Daniel R. Weinberger, M.D., Chief of the Clinical Brain Disorders Branch of the NIMH.

The Samuel G. Hibbs Award was presented to Charles B. Nemeroff, M.D., Chief of the Division of Biological Psychiatry at Duke University, for his paper entitled "The Thyroid Axis in Depression: Pathophysiological and Clinical Implications." This award is given for the best unpublished paper on a clinical subject.

The Blanche F. Ittleson Award for Research in Child Psychiatry, given to a child psychiatrist or group of investigators for published results of research pertaining to the mental health of children, was presented to Professor Michael L. Rutter, Professor and Head of the Department of Child and Adolescent Psychiatry at the Institute of Psychiatry in London, England.

The Kempf Fund Awards for Research Development in Psychobiological Psychiatry were presented to Neal R. Swerdlow, M.D., a psychiatrist resident at the University of California, San Diego School of Medicine, to honor a resident who demonstrates exceptional promise in psychiatric research; and to David L. Braff, M.D., the University of California, San Diego, for significant contributions to research in the physiological, psychological, and/or sociological causes and treatment for the mental diseases known as schizophrenia.

Dennis P. Cantwell, M.D., Joseph Campbell Professor of Psychiatry and Director of Training in Child Psychiatry at the UCLA Neuropsychiatric Institute, received the Agnes Purcell McGavin Award, given to honor a psychiatrist who has done and is currently doing outstanding work related to the preventive aspects of the emotional disorders of childhood, through framing concepts, developing proofs or creating applications.

The Robert T. Morse Writers Awards, which honors popular writers who have made major contributions to the public understanding of psychiatry and mental illness, were presented to Mr. Lawrence K. Beaupre, Vice-President and Executive Editor of the Westchester Rockland Newspapers; and to Ms. Erica E. Goode, senior editor for Behavioral Sciences at *U.S. News and World Report*.

Robert Coles, M.D., psychiatrist and Pulitzer Prize winning author, received the Oskar Pfister Award, given to honor outstanding contributions in the field of psychiatry and religion.

The Psychiatric Institutes of America Foundation Award for Research Development in Hospital Psychiatry, given to honor outstanding contributions in hospital psychiatry research, was presented to Mark Olsson, M.D., of the Payne Whitney Psychiatric Clinic at Cornell University Medical College; and to Howard H. Goldman, M.D., Professor of Psychiatry and Director of Mental Health Policy Studies at the University of Maryland School of Medicine in Baltimore.

The Robert L. Robinson Award was given to Hugh Downs, host of ABC News "20/20" and Jonathan Talmadge, writer, producer and reporter for ABC News, for their work on the program "Depression: Beyond the Darkness"; and to Jerry Sander, medical reporter at WKYT-TV for his work on the program "Manic Depression." The Robert L. Robinson Award recognizes radio and television (including cable) productions that contribute significantly to a better public understanding of psychiatry and mental illness.

The Arnold L. van Ameringen Award in Psychiatric Rehabilitation was presented to the National Alliance for the Mentally Ill, for its outstanding contributions to the field of psychiatric rehabilitation, in the areas of service, research, education, advocacy or a combination thereof. The award was accepted by Laurie M. Flynn, M.A., Executive Director of NAMI.

The Seymour D. Vestermark Award, which recognizes an educator who has made outstanding contributions to undergraduate, graduate, or postgraduate education and career development in psychiatry, was presented to Charles A. Pinderhughes, M.D., Associate Chief of Staff for Education at the Edith Nourse Rogers Memorial Veterans Hospital in Bedford, MA.

The Jack Weinberg Memorial Award for Geriatric Psychiatry was presented to Ralph J. Kahana, M.D., Associate Clinical Professor of Psychiatry, Harvard Medical School. This award honors a psychiatrist who has demonstrated special leadership or who has done outstanding work in clinical practice, training or research into geriatric psychiatry anywhere in the world.

After the presentation of these awards, Dr. Benedek adjourned the Convocation.

Awards presented at meetings or sessions other than the Convocation included the following:

District Branch Newsletter of the Year Awards, given to recognize excellence in achievement and honor those newsletters and their editors that have most effectively communicated with the District Branch membership. The award for Large District Branches was presented to the *IPS Report*, Richard K. Baer, M.D., and David Spiegel, M.D., Editors; and for Small District Branches, *PMA Newsletter*, Kathy Barrett, Editor. The Continuing Excellence Award was presented to *APS Action*, James F. Hooper, M.D., Editor; *Connecticut Psychiatrist*, Boris Rifkin, M.D., Editor; and *Pennsylvania Psychiatrist*, Denis Milke, M.D., Editor.

The Manfred S. Guttmacher Award, given to honor outstanding contributions to the literature of forensic psychiatry, was given to Alan W. Schefflin, LL.M., Professor of Law at Santa Clara University Law School, and to Jerrold Lee Shapiro, Ph.D., Associate Professor of Counseling Psychology at Santa Clara University.

The Lilly Psychiatric Research Fellowship was awarded to Robert T. Malison, M.D., Chief Resident on the Clinical Neuroscience Research Unit at Yale University. The fellowship was established to provide support for the career development of a postgraduate medical trainee who has shown exceptional promise in psychiatric research.

The Adolf Meyer Award honors outstanding investigators and was awarded to Daniel X. Freedman, M.D., Acting Chairman of the Department of Psychiatry and Biobehavioral Sciences at UCLA and Acting Director of the UCLA Neuropsychiatric Institute.

The Award For Patient Advocacy, which recognizes a public figure respected for personal accomplishments and beliefs, who has promoted the improvement of services for people coping with mental disorders and substance abuse, and who has fought stigma by speaking out about experiences with mental illness and psychiatric treatment, was awarded to Temple Grandin, Ph.D., Assistant Professor in the Department of Animal Sciences at Colorado State University and an independent livestock handling consultant who was a partially autistic child.

The Benjamin Rush Award, which honors an individual who has achieved renown for his/her contribution to the history of psychiatry from that field or other fields such as medical history, anthropology or sociology, was awarded to Stanley W. Jackson, M.D., Professor of Psychiatry and the History of Medicine at Yale University and a faculty member at the Western New England Institute for Psychoanalysis.

The Simon Bolivar Award, which is given to honor a prominent Hispanic statesman or spokesperson, was awarded to Pedro Ruiz, M.D., Professor of Psychiatry at Baylor College of Medicine and Chief of the Psychiatry Service at Ben Taub General Hospital in Houston.

Evelyn K. Moore, M.A., Executive Director and a founding member of the National Black Child Development Institute, received the Solomon Carter Fuller Award Lecture, given to honor a Black citizen who has pioneered in an area which has significantly benefited the quality of life for Black people.

The Jacob K. Javits Public Service Award, which honors a public servant who has made a significant contribution to the cause of the mentally ill, was received by The Honorable Pete V. Domenici.

Scientific Sessions

The Scientific Program began on Monday, May 13, but continuing medical education (CME) courses and industry sponsored symposia began on Saturday and Sunday, May 11-12. There were 22 discussion groups; six forums; 100 symposia; 20 industry sponsored symposia; two special presidential symposia; 660 new research presentations; two debates; one "round table discussion"; 135 papers presented in 45 paper sessions; 137 workshops (including 60 APA component presentations and 77 issue); 17 film sessions; 25 videotape sessions and three video production clinics; 103 CME courses; four medical updates; five review of psychiatry sessions; four clinical case conferences; two, two-part continuous clinical case conferences; three "research consultations with . . ." sessions; and twelve "clinical consultations with . . ." sessions. Other sessions included "Research Advances in Psychiatry: An Update for the Clinician"; "Workshops on Private Practice Issues"; the residents' session, "Meet the Experts: Sunny-Side Up"; the NIMH Workshop; the DSM-IV Update; the Pub-

lic Symposium; the Social Security Workshop; and an AIDS Program and Resource Center.

There were 31 lectures presented. The speakers, their current positions, and the titles of their presentations are listed here.

On Monday, May 13, the following speakers gave lectures: Daniel X. Freedman, M.D., Past President of the American Psychiatric Association, Judson Braun Professor of Psychiatry and Pharmacology at the University of California, Los Angeles, "The Search: Body, Mind and Human Purpose"; Albert J. Solnit, M.D., former Sterling Professor of Pediatrics and Psychiatry at Yale University School of Medicine and Child Study Center, "Truth Telling: The Child as Witness"; Professor Mingdao Zhang, Vice-Director of the Shanghai Institute of Mental Health and of the World Health Organization Collaborating Center for Research and Training in Mental Health in Shanghai, "Mental Health Services in Shanghai, China"; Daniel N. Stern, M.D., Professor of Psychology at the University of Geneva in Switzerland, "Infancy: A Theoretical Playground for the Study of Mind"; Antoinette Parisi Eaton, M.D., President of the American Academy of Pediatrics, "The American Academy of Pediatrics' National Agenda: A Blueprint for Action."

On Tuesday, May 14, the following lectures were given: Charles A. Pinderhughes, M.D., Associate Chief of Staff for Education at the Edith Nourse Rogers Memorial Veterans Hospital in Bedford, Massachusetts, "The Dual Personalities in Therapists and Patients"; Paul H. Ornstein, M.D., Professor of Psychiatry at the University of Cincinnati College of Medicine, "The Clinical Impact of the Psychotherapist's View of Human Nature"; Robert Coles, M.D., a research psychiatrist for the Harvard University Health Services, "The Moral and Spiritual Life of Children"; Stanley W. Jackson, M.D., Professor of Psychiatry and the History of Medicine at Yale University, "The Listening Healer in the History of Psychological Healing"; Joel J. Elkes, M.D., Director of the Division of Attitudinal and Behavioral Medicine, "Psychobiology and Communications: Psychiatry and the Future of Medicine"; Stuart C. Yudofsky, M.D., Professor and Chairman of the Department of Psychiatry at the University of Chicago and Robert E. Hales, M.D., Chairman of the Department of Psychiatry at Pacific Presbyterian Medical Center, "The Role of Neuropsychiatry in Psychiatry's Future"; James M. McPherson, Ph.D., author of the Pulitzer Prize winner *Battle Cry of Freedom: The Civil War Era*, hailed as the best one-volume history of the Civil War ever written, "Why They Fought: Ideology and Combat Motivation in the Civil War"; Pedro Ruiz, M.D., Professor of Psychiatry at Baylor College of Medicine, "The Hispanic-American Substance Abuser: Problems and Perspectives"; Herbert D. Kleber, M.D., Deputy Director for Demand Reduction at the Office of National Drug Control Policy, "The Rise and Decline of the American Cocaine Epidemic: A Psychiatrist and Policymakers's Perspective"; Ambassador Tahseen Basheer, former Ambassador to Canada from Egypt, Lecturer on Foreign and Middle East Affairs at the Egyptian Diplomatic Institute, "The Gulf Crisis: An Egyptian Perspective."

On Wednesday, May 15, the following lectures were presented: Pasko Rakic, M.D., Professor of Neuroscience at Yale University School of Medicine, "Genetic and Epigenetic Control of Cortical Function"; Jimmie C. Holland, M.D., Chief of the Psychiatry Service at Memorial Sloan-Kettering Cancer Center, "Psychooncology: Cancer's Newest Subspecialty"; Frederick K. Goodwin, M.D., Administrator of the Alcohol, Drug Abuse, and Mental Health Administration, "Psychiatry in the 1990s: Leadership for Medicine and Biomedical Science"; T. Berry Brazelton, M.D., Clinical Professor of Pediatrics at Harvard Medical School, "Why is America Failing Our

Children?"; Charles B. Nemeroff, M.D., Chief of the Division of Biological Psychiatry, Professor of Psychiatry and Pharmacology at Duke University Medical Center, "The Thyroid Axis in Depression: Pathophysiological and Clinical Implications"; Bruce S. McEwen, Ph.D., Professor and Head of the Laboratory of Neuroendocrinology and Associate Dean for Graduate and Postgraduate Studies at Rockefeller University, "Paradoxical Effects of Adrenal Steroids on the Brain: Plasticity Versus Degeneration"; Professor Juan Ramon de la Fuente, M.D., Dean of Faculty of Medicine at the National University of Mexico, "Under the Volcano: Alcohol Related Problems Across the Border"; Mihaly Csikszentmihalyi, Ph.D., Professor of Human Development and Education, Department of Psychology, University of Chicago, "Experience Sampling: How To Measure the Quality of Life"; Felton J. Earls, M.D., Professor of Child Psychiatry at Harvard Medical School, "Violence and the American Scene: 1990 to 2000"; Dr. Semyon F. Gluzman, a Soviet psychiatrist internationally renowned for his opposition to the political use of psychiatry, "The Effects of Political Realities on Psychiatry in the USSR"; Lewis L. Judd, M.D., former Director of the National Institute of Mental Health, Professor and Chairman of the Department of Psychiatry at the University of California, San Diego School of Medicine, "Mental Illness, Stigma and the Failure to Achieve Parity: What Psychiatry Must Do."

The lectures presented on Thursday, May 16, were: Evelyn K. Moore, M.A., Executive Director of the National Black Child Development Institute, "Our Children: Miles to Go, Promises to Keep: The Future is Now"; Jack F. Wilder, M.D., Director of the Mental Health Education Program at the Albert Einstein College of Medicine at Yeshiva University in the Bronx, New York, "Weekend with 2,000 Chief Residents: Implications for Training"; James D. Watson, Ph.D., Professor of Biology at Harvard University, "The Evolution of DNA: From Double Helix to the Human Genome Project"; Temple Grandin, Ph.D., once an autistic child, now Assistant Professor in the Department of Animal Sciences at Colorado State University, "My Personal Experience: Autistic Child to Adult Scientist."

Other Activities

The Committee on Local Arrangements, Daniel K. Winstead, M.D., chairperson, planned many activities, among which were golf and tennis tournaments, fishing, biking, stargazing and birdwatching. Some of the tours included: Audubon Riverboat to the Zoo, Louisiana Swamp Tour with a Casual Cajun Lunch, Garden District Residential Tour with Lunch at Commander's Palace and African-American Heritage in New Orleans. Many special tours planned just for children were also presented, including Mardi Gras World and the Superdome, Cafe du Monde and the Louisiana Nature Center, and Dinner at the Hard Rock Cafe and Bowling.

Meeting of the Board of Trustees

The Board of Trustees met in regular session on Sunday, May 12.

Meetings of the Assembly

The Assembly met on Friday, Saturday, and Sunday, May 10, 11, and 12.

PHILIP M. MARGOLIS, M.D.
Secretary, American Psychiatric Association

Position Statement on HIV and Youth

This statement was proposed by the Commission on AIDS.¹ It was approved by the Board of Trustees in March 1991 and by the Assembly of District Branches in May 1991.

The HIV epidemic is an unprecedented threat to youth. We cannot take comfort in the deceptively small numbers of children and adolescents thus far identified as HIV-infected.

Homelessness, family dysfunction, substance abuse, and physical, sexual, and emotional abuse, coupled with sexual maturation and progressive emancipation, have created a population of vulnerable adolescents at risk for HIV infection. In addition, increasing numbers of HIV-positive women, many of whom are themselves teenagers, are bearing children who may be HIV-infected.

Reported correlates of HIV risk behavior among adolescents include poor school attendance, use of drugs or alcohol, early onset of sexual activity, and inadequate adult supervision.

Many studies have verified that changes in knowledge about HIV are not, by themselves, sufficient to bring about changes in HIV risk behavior. Reduction of HIV risk behavior is achievable but requires interventions that are intensive, multifaceted, and long-term.

To meet this crisis, efforts to modify attitudes and behavior are needed at multiple developmental stages, and reinforcement should

be given by parents, peers, and health care professionals, as well as teachers and the media.

APA urges its members and other health care professionals to do the following.

1. Acquire, through clinical experience when feasible, basic medical knowledge and skills relevant to HIV, including its impact on children, adolescents, and families.
2. Support and participate in HIV prevention activities:
 - a) Educational interventions that begin early in childhood, target parents and families as well as children in schools, and provide culturally appropriate sex and health education geared to each age level.
 - b) Effective HIV risk reduction programs for all adolescents.
 - c) HIV risk reduction programs that address the particular needs of racial, ethnic, and sexual minorities, as well as homeless, abused, learning disabled, and mentally ill children and adolescents.
3. Support research efforts directed at learning how the impact of HIV on children, adolescents, and families can be ameliorated and how transmission of HIV to and among young people can be reduced.
4. Advocate a commitment of adequate resources, both nationally and locally, to address the societal problems that underlie HIV risk behaviors.
5. Incorporate messages and attitudes into psychiatric practice that promote the reduction of HIV risk behaviors.

¹ The Commission on AIDS includes James Krajewski, M.D. (chairperson), Jeffrey Akman, M.D., Alexandra Beckett, M.D., Francisco Fernandez, M.D., Janice Hutchinson, M.D., Joyce Johnson, D.O., Eric Kaplan, M.D., Robert Kertzner, M.D., Stuart Nichols, M.D., David Rosmarin, M.D., Jacqueline Etemad, M.D., Simon Auster, M.D. (corresponding member), Ruth Herman, M.D. (APA/Burroughs Wellcome Fellow), Eric Bing, M.D. (APA/NIMH Fellow), Douglas Sargent, M.D. (Board liaison), and James Nininger, M.D. (Assembly liaison).

A Challenge for Psychiatry

As psychiatrists, we function primarily as observers and change agents of human behavior. Throughout our training and professional careers, objectivity is a standard that we strive to maintain as we deal with transference issues and attempt to help our patients to the greatest extent possible.

However, there are many instances when circumstances challenge both our objectivity and our capacity to maintain a proper distance from the situation that we have been called upon to resolve. At those times, we often find ourselves in the position of being more of an actor in a play than a member of the audience.

Dr. Neumann's paper, "Psychiatry in Eastern Europe Today: Mental Health Status, Policies, and Practices," published in this issue of the *Journal*, focuses our attention on what can happen when the "patient" may be the society in which we live, the mental health system within which we work, or an individual on whom we depend for our very livelihood and life. At such times, it may not be so easy for a psychiatrist to maintain objectivity and to remain neutral.

Although psychiatrists in the United States may wish to see themselves as being distant from the social and political changes that have occurred in recent years in Eastern Europe, the distance may not be so great as we would like to think or believe.

Dr. Neumann describes in his paper the impact of these changes on the role of psychiatrists, the nature of psychiatric education and care, and the status of psychiatrists within a society and culture. I hope that, rather than being perceived as a first-person narrative from another world of no more than passing curiosity, his views will serve as a stimulus for each of us to examine our own actions and reactions in "similar" situations.

Consider for a moment the dilemmas faced by psychiatrists in the United States who are employed, often in the public sector, in institutions where the working conditions and the therapeutic environments are less than satisfactory.

Consider for a moment the dilemmas faced by psychiatrists, often in private practice, who are asked to act in a manner contrary to good clinical judgment or ethical standards because the patient is a VIP.

Consider for a moment the dilemmas faced by socially conscious psychiatrists who view their government as pursuing policies that are contrary to the promotion of good mental health and who then speak out at the risk of losing both their professional and community standing.

What Dr. Neumann tells us through his descriptions of psychiatric life in his homeland and other similar countries is that, under these and other similar conditions, he and his colleagues have reacted in widely different ways. In the aftermath of the "liberation" of Eastern Europe, each of us must ask ourselves how we wish to respond to the ethical dilemmas that many of our colleagues faced in recent years.

Do we wish to require that those who acted contrary to ethical professional standards now face some type of professional tribunal as to the appropriateness of their actions? Or do we wish to acknowledge and then "forgive" their actions, recognizing that it will serve little purpose to "prosecute" those who have erred in the past and only delay the restoration of an ethically functioning psychiatric community?

Whatever our individual decisions, it behooves us as psychiatrists whose professional tools include understanding and compassion to first reflect about whether their actions may have been the only recourse available to them at that time and what the nature of the "choice" was that they had when undertaking those actions.

Dr. Neumann is clear about how he hopes we will try to resolve this dilemma. He is asking each of us to extend a helping hand, as well as an understanding heart, to our colleagues in these countries if they now demonstrate a willingness to join a new community of psychiatrists, dedicated to a different way of practice under a very different set of political and social conditions.

If U.S. psychiatrists are to be members of a worldwide community of psychiatrists, then we must include within our individual and collective agendas an openness to understanding the new circumstances of our colleagues in Eastern Europe and a willingness to assist them in making the changes that they now wish to make.

As Dr. Neumann points out, this task of reform will not be easy or short-term. It will require a long-term commitment, technical and financial assistance, and, most of all, the participation of many psychiatrists as teachers and consultants. APA, as our organizational representative, can also play an important role by developing a plan and assisting with its implementation. In view of the kinship that we should feel with the experiences and circumstances of our colleagues, this does not seem to be an unreasonable request. Only time will tell if it is.

ALLAN BEIGEL, M.D.

Dr. Beigel is Professor of Psychiatry and Psychology and Vice-President for University Affairs of The University of Arizona in Tucson. He also serves as Secretary for Sections of the World Psychiatric Association. Address reprint requests to him at The University of Arizona, Administration Bldg. 702, Tucson, AZ 85721.

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Substance Abuse Disorders: A Psychiatric Priority

Group for the Advancement of Psychiatry
Committee on Alcoholism and the Addictions

The renewed public, governmental, and professional interest in addictive disorders should serve to encourage the interest of psychiatrists in this important and rapidly changing field. It is the view of the Group for the Advancement of Psychiatry (GAP) Committee on Alcoholism and the Addictions that all psychiatrists should possess expertise in the recognition, assessment, and treatment of substance use disorders. This position paper by the GAP committee reviews the role of the psychiatrist in the evaluation and treatment of patients with substance use disorders. It also notes some of the obstacles to full involvement in this field by medical practitioners in general and psychiatrists in particular. The psychiatrist has a critical role to play in the diagnosis and treatment of patients with substance use disorders. As biopsychosocial phenomena, substance abuse problems constitute a special and direct challenge to the psychiatrist, whose training, perspective, and competence should span all three domains. Psychiatrists must be willing to accept this challenge and fully participate in the development and application of treatment strategies adequate to cope with the enormous human suffering resulting from the abuse of alcohol and other psychoactive drugs.

(Am J Psychiatry 1991; 148:1291-1300)

It is estimated that one out of seven people in the United States abuse or are dependent on alcohol and that an additional one out of 20 individuals abuse or are dependent on other drugs (1). The morbidity and mortality resulting from substance abuse is impressive. For example, in 1980, 69,000 deaths in the United States were directly attributed to alcohol abuse and an additional 6,000 deaths were attributed to drug abuse (2). The economic consequences are also impressive. In

1983, the estimated cost of alcohol and drug abuse to the U.S. economy was \$177.4 billion, more than two and a half times the estimated economic cost of all other mental disorders combined (3). Of this amount, approximately 60% was the result of reduced productivity, lost employment, and the socioeconomic sequelae of disrupted lives and relationships among substance abusers. The role of substance abuse in the genesis and perpetuation of accidents, violence, and homelessness adds to this toll (3, 4).

With respect to the mental health implications of substance abuse, several studies have demonstrated higher prevalence rates of substance use disorders among psychiatric patients than in the general population (5) as well as high prevalence rates of psychiatric disorders among patients with substance abuse problems (6, 7). In addition, clinical data reveal that many patients seeking psychiatric care have been adversely affected by substance abuse in a significant other, notably a parent or spouse.

Despite the enormous personal and social cost of substance abuse, public concern and the interest of the

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The Committee on Alcoholism and the Addictions is made up of Edward J. Khantzian, M.D., Chairman, Margaret Bean-Bayog, M.D., Susan Blumenthal, M.D., Richard Frances, M.D., Marc Galanter, M.D., Earl Loomis, M.D., Sheldon I. Miller, M.D., Robert Millman, M.D., Steven Mirin, M.D., Edgar Nace, M.D., Norman Paul, M.D., Peter Steinglass, M.D., John Tamerin, M.D., Joseph Westermeyer, M.D., Ph.D., Alexander D. Kalogerakis, M.D., John Menninger, M.D., and James Coleman.

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medical profession in this problem have waxed and waned. However, the recent epidemic of cocaine abuse and the rapid spread of HIV infection among intravenous drug users (8) have reawakened the nation, and the mental health profession, to the enormous public health implications of substance abuse and dependence. In response to public concern, Congress and the Executive Branch have approved major increases in the budgets of the National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism for treatment, research, and education efforts in this area. At the same time, the federal effort to reduce both the supply and demand for addictive substances has been renewed, with the help of a massive increase in funding for this purpose (9).

Unfortunately, psychiatry, as a discipline, has been relatively slow to respond to the need for expanded treatment, research, and teaching in the area of drug and alcohol addiction. Within the treatment system, "addictionologists" of all disciplines have supplanted psychiatrists on the front lines. In education, the demise of the federally supported Career Teacher Program in the Addictions has slowed the momentum toward inclusion of teaching about addictive disorders in medical school curricula and residency training programs. In the research arena, there is a clear need to increase funding for physician researchers (10).

On a more positive note, APA has recently responded to the need for visible leadership in this area by creating the Council on Addiction Psychiatry. The recently formed American Academy of Psychiatrists in Alcoholism and Addictions now numbers more than 1,000 members, and the Group for the Advancement of Psychiatry (GAP) now has a Committee on Alcoholism and the Addictions. In the area of training, more than 40 centers now offer postgraduate fellowships in this field, and the American Board of Psychiatry and Neurology (ABPN) has recently recommended designating addiction psychiatry as an area in which added qualifications can be recognized through subspecialty certification.

The renewed public, governmental, and professional interest in addictive disorders should serve to encourage the interest of psychiatrists in this important and rapidly changing field. Indeed, it is our view that all psychiatrists, regardless of subspecialty interest, should possess expertise in the recognition, assessment, and treatment of substance use disorders. This position paper by the GAP Committee on Alcoholism and the Addictions reviews the role of the psychiatrist in the evaluation and treatment of patients with substance use disorders.

SELECTIVE ISSUES IN THE ASSESSMENT OF PATIENTS WITH SUBSTANCE USE DISORDERS

Important Commonalities

As a group, substance use disorders share some important commonalities. In addition to the biological and

behavioral sequelae of drug intoxication or withdrawal, drugs of abuse and the associated drug-using life style have profound effects on cognitive development, personality organization, and interpersonal relationships as well as on the user's ability to cope with stress and to conform to social norms and mores. Thus, it is not surprising that the current diagnostic criteria for substance use disorders elucidated in *DSM-III-R* include not only the classic hallmarks of addiction (e.g., drug tolerance, abstinence symptoms, withdrawal), but also the wide-ranging effects of addicting substances on behavior and social functioning.

For the psychiatric practitioner, the assessment of patients with substance use disorders is facilitated by understanding that the addictive state is defined by phenomena which transcend the specific pharmacological properties of the drugs themselves. There is a "generic" aspect to the substance use disorder that is reflected in both the clinical presentation of these patients and in their subsequent management. Common clinical phenomena include physical and psychological dependence, the presence of variable degrees of drug craving, preoccupation with obtaining and using drugs, and loss of control over drug consumption. Cognitively, there is an erosion in one's confidence—a fear of being unable to function without being intoxicated and of being unable to abstain from drug use. Decrements in work performance, failed relationships, and overt acts of negligence are overlooked and/or supported by pathological psychic defenses, including denial, projection, rationalization, and grandiosity.

Etiologic Factors

In considering the etiology of substance use disorders, the practitioner must bear in mind that psychosocial and biogenetic factors interact in a multifactorial framework in the pathogenesis of these disorders.

Psychosocial factors. Early psychoanalytic formulations have variously focused on drug abuse or dependence as a symptom of depression (11), a manifestation of oral regression (12), a masturbatory equivalent (13), or a defense against homosexuality (14). More modern psychodynamic theorists have espoused a self-medication paradigm based on the hypothesized role of psychoactive drugs in regulating unpleasant affects and as an expression of deficiencies in self-care (15–18). Systems theorists have studied the role of familial dysfunction in the development of addictive disorders (19), and social scientists have emphasized the role of cultural mores in this process (20).

The role of genetic heritability. Studies of twins (21), adoptees (22), and siblings raised apart (23) have clearly demonstrated the importance of genetic factors in the transmission of alcoholism (24), but the role of genetic factors in the development of other substance use disorders has not been well studied. Attempts to separate environmental from genetic factors in the development of alcoholism are being carried out (25), and efforts to map the gene or genes that convey a vulner-

ability to alcoholism are also underway (26). Among the latter is the search for possible biological markers of this disorder, measures of differential alcohol tolerance, response to alcohol challenge, the effects of alcohol on platelet monoamine oxidase activity, and evoked potential studies in alcoholics and/or their offspring compared with appropriate control groups (24). These and other studies may eventually lead to a greater understanding of the pathophysiology of alcoholism and of the peculiar vulnerability of alcoholics to the subjective effects of this drug.

Neurobiological mechanisms. Drugs of abuse vary a great deal in the subjective effects that, by and large, are mediated through their actions on brain neurotransmitter systems (27). Some directly affect excitatory noradrenergic neuronal pathways in the CNS, particularly those pathways which arise from the locus ceruleus and terminate in the limbic system and cerebral cortex and/or dopaminergic neurons in the mesolimbic area (28). For example, cocaine and other CNS stimulants affect both noradrenergic and dopaminergic neuronal systems by facilitating the release of these catecholamines from presynaptic neurons, as well as by inhibiting the neuronal reuptake of these neurotransmitters (29). These actions are thought to constitute the neurobiological mechanism by which stimulant drugs produce euphoria, hyperactivity, and other reinforcing effects following acute administration.

Chronic use of drugs like cocaine has been found to result in depletion of brain stores of norepinephrine and dopamine with an accompanying increase in postsynaptic receptor sensitivity (29), and it has been postulated that depletion of these catecholamines may be responsible for the depression that accompanies cocaine withdrawal. It has also been postulated that changes in dopamine receptor sensitivity may contribute to cocaine craving. These theories provide the basis for new treatments that may prove to be effective in reducing depression and/or cocaine craving following cocaine withdrawal (30). These include the blockade of catecholamine reuptake with tricyclic antidepressants (31) or the reduction of dopamine receptor sensitivity with administration of dopamine agonists (32).

In the case of opiates, chronic administration has been found to reduce noradrenergic tone in the CNS, and abrupt withdrawal results in noradrenergic hyperactivity in both the CNS and the peripheral autonomic nervous system. Clonidine, a specific α_2 receptor agonist, reduces the firing rate of presynaptic neurons and, by so doing, ameliorates the noradrenergic hyperactivity that accompanies opiate withdrawal (33).

Finally, the subjective effects of alcohol and the benzodiazepines are also mediated by the action of these drugs on brain neurotransmitters and their receptor sites. Specifically, alcohol enhances the neuronal activity of γ -aminobutyric acid (GABA), a brain neurotransmitter, which counters the excitatory effects of norepinephrine. An increased flow of chloride ions across the GABA/benzodiazepine receptor membrane results in the membrane hyperpolarization that is thought to un-

derlie the anxiolytic activity of alcohol, the benzodiazepines, and other CNS depressants (34).

Psychiatric Comorbidity in Substance Abusers

Although many of the observed changes in behavior, mood, and cognition that result from drug and/or alcohol abuse resolve when addicts are detoxified and remain drug free, in some patients, signs and symptoms suggestive of an associated psychiatric disorder (e.g., depression) persist long after abstinence has been achieved. This finding, coupled with the observation that most users prefer specific classes of drugs (e.g., stimulants versus depressants) suggests that some individuals may be attempting to self-medicate a concurrent psychiatric disorder with drugs or alcohol (18). In this context, diagnostic studies reveal differential rates of concurrent axis I disorders among specific drug-using subgroups (6). Data from such studies must be viewed with caution, however, because there is considerable variability in the methods used for arriving at a diagnosis (e.g., clinical impression versus structured interview), the specific diagnostic criteria employed, and the time point at which diagnostic judgments were made (e.g., at admission versus 3 months after detoxification).

These caveats notwithstanding, a series of reports between 1975 and 1985 have documented a consistently high rate of depression among substance abusers. Among opiate addicts, one-third to one-half were found to meet *DSM-III* criteria or Research Diagnostic Criteria for major depression at the time of evaluation, and up to two-thirds met criteria for a diagnosis of depressive disorder (mostly unipolar) at some point in their lives (35–39). In addition, most studies have reported a high rate of axis II disorders in these patients, particularly antisocial personality disorder (38, 39).

Similarly, diagnostic studies in cocaine abusers suggest that these individuals have a high prevalence rate of concurrent depression, bipolar disorder, and attention deficit disorder (40–43), compared with the general population and users of other drugs. Axis II personality disorders are also quite common, predominantly narcissistic, histrionic, or borderline types. In addition, Weiss et al. (44) have reported a higher prevalence of antisocial personality disorder in these patients.

Most studies of alcoholics report a high prevalence of concurrent affective illness and anxiety disorders compared with the general population (45, 46). Weiss and Rosenberg (47) found that 40% of patients presenting for treatment of alcohol abuse and/or dependence were also suffering from some form of affective disorder. Conversely, 30% to 40% of patients presenting for treatment of affective disorders have abused alcohol or other depressant drugs (47). Furthermore, individuals who abuse alcohol and other CNS depressants appear to have relatively higher rates of anxiety disorders than opiate or cocaine abusers (46, 47). However, in the cited and similar studies, it was often unclear which condition was primary or whether the psychopathology

was the cause or consequence of alcoholism. Schuckit et al. (48, 49) reported that much of the depression and anxiety associated with alcoholism cleared with abstinence. The importance of differentiating diagnostic syndromes (i.e., disorders) from transient psychiatric symptoms that recede with abstinence is important because the presence of co-occurring, persistent psychiatric disorders has important prognostic and treatment implications (6, 46).

Finally, alcoholics also appear to have higher rates of personality disorder than the general population (50). In the Epidemiologic Catchment Area survey, antisocial personality disorder was strongly associated with alcoholism (7). Indeed, individuals with antisocial personality disorder were 21 times more likely to have a diagnosis of alcoholism than were individuals without antisocial personality disorders. Meyer (51) reported that the concurrent presence of antisocial personality disorder in an alcoholic patient is associated with earlier onset and poorer prognosis.

In summary, the evidence to date suggests an intricate and not entirely uniform set of relationships between various patterns of drug abuse and the concurrent presence of other psychiatric disorders. The challenge for the future is to develop reliable methods for defining the precise temporal and etiologic relationships between drug use and other forms of psychopathology and then to devise treatment programs that specifically address each of the disorders present.

Substance Abuse Disorders and Suicide

The relationship between substance abuse and suicidal behavior has been well documented. Indeed, the incidence of suicide among drug abusers is about 20 times that in the general population (52), and as many as 70% of suicides in young people are associated in some way with substance abuse (53). Alcohol abuse is a factor in 25% to 50% of all suicides (54), including those by nonalcoholics. Among alcoholics, estimates vary, but somewhere between 5% and 27% of all deaths are caused by suicide, and the lifetime risk of suicide is estimated to be about 15% (55). In the general population, alcohol is second only to affective disorder as a risk factor in suicide.

The impetus for suicide in substance-abusing patients is frequently related to issues of personal loss, humiliation, the medical and psychiatric problems that accompany these disorders, and the acute disinhibiting effects of the drug itself (54, 55). However, recent findings of low CSF levels of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) in individuals who have attempted suicide, in the brains of suicide victims (56), and in some alcoholics (57) suggest a possible link between alcoholism abnormalities in brain neurochemistry and suicidal behavior. These findings may also have implications for pharmacological interventions, including the use of serotonin reuptake blockers in alcoholics who are thought to be at risk for suicide.

Organic Brain Syndromes Associated With Substance Abuse

Following acute use. A variety of organic psychiatric syndromes may emerge during acute or chronic drug use or during drug withdrawal. *DSM-III-R* currently delineates seven distinct organic syndromes involving 11 classes of psychoactive substances. The most common of these is intoxication, which is produced by all classes of drugs except nicotine. Some drugs, like the opioids, inhalants, and caffeine, produce intoxication without any other acute syndromes. At the other end of the spectrum, high doses of amphetamines, cocaine, and phencyclidine (PCP) may produce an organic delirium of variable duration. This delirium is usually brief (up to 6 hours) after amphetamine or cocaine use but lasts longer (1 to 7 days) after PCP use. Changes in the naming system for *DSM-IV* are currently being considered. It is anticipated that the new diagnoses for organic brain syndromes associated with substance abuse will have a three-part name indicating drug, state, and syndrome (e.g., cocaine intoxication psychosis). This change will help guide clinicians in ascertaining treatment requirements by indicating whether a state is intoxication, withdrawal, or persistent (T.J. Crowley, personal communication).

Acute use of amphetamines, cocaine, or PCP may result in a delusional state that is usually brief, lasting from several hours to several days. In some patients, however, it may last up to a year, even in the absence of further drug use. Hallucinogen use has also been associated with the development of a delusional disorder that is sometimes difficult to distinguish from schizophreniform illness (58). Brief psychotic reactions following cannabis use have also been reported (59).

Following chronic use: withdrawal syndromes. With the exception of the hallucinogens, PCP, and the inhalants, prolonged drug or alcohol use is accompanied by the development of drug tolerance and physical dependence. Consequently, abrupt cessation of use under these conditions will be followed by a characteristic withdrawal syndrome. In the case of withdrawal from CNS depressants (i.e., alcohol, barbiturates, and benzodiazepines), tremulousness, diaphoresis, palpitation, anxiety, and irritability may give way to life-threatening seizures and delirium. Opioid withdrawal, although often uncomfortable, is not life threatening, except in addicted newborns. Abrupt withdrawal from cocaine and other stimulants may be accompanied by a "crash," characterized by depression, fatigue, increased need for sleep, and increased appetite (60). A recent report by Weddington et al. (61) suggested, however, that cocaine addicts may not experience pronounced withdrawal symptoms. A mild withdrawal syndrome following chronic high-dose marijuana use has also been described (62). It is characterized by irritability, anxiety, insomnia, nausea, and anorexia.

Protracted withdrawal states also occur. These often go unrecognized or their signs and symptoms are attributed to other psychiatric disorders. Examples include

the prolonged depression that may occur following withdrawal from opioids, alcohol, or cocaine and the irritability and anxiety that may be part of a prolonged abstinence syndrome following cessation of alcohol, opiate, or nicotine use (63).

Following chronic use: other neuropsychiatric sequelae. Psychiatric syndromes that persist beyond acute or chronic withdrawal are, in some instances, permanent. They include alcohol dementia, alcohol amnesic disorder, persistent insomnia, and a variety of chronic depressive states (64). Less common are post-hallucinogen perception disorder, alcoholic hallucinosis, and chronic psychosis associated with extensive stimulant (PCP) or hallucinogen abuse (65). These organic conditions must be distinguished from psychiatric and neurological syndromes unrelated to substance abuse as well as other factors such as metabolic conditions, liver disease, and nutritional deficits. The impact of drug-induced organic brain syndromes and protracted withdrawal states on personality is an area in need of further study.

AIDS and Substance Abuse

Needle sharing among intravenous drug users as well as high-risk sexual practices among drug abusers of all types contribute to a higher risk of AIDS in this population.

As of September 1989, there were 21,188 reported cases of HIV infection in intravenous drug users, representing 21% of all AIDS cases in the United States. Among the 9,724 women who had been diagnosed with AIDS by that date, 51% were intravenous drug users and an additional 19% were the sexual partners of intravenous drug users. Of the 1,859 children diagnosed with AIDS, 58% had mothers who had used drugs intravenously or were the sex partners of intravenous drug users (66).

Intravenous drug users constitute the second leading risk group for infection with the HIV virus and are the primary vector for transmission of the disease to the adult heterosexual and pediatric populations (66). There is, however, considerable geographical variation in the prevalence of seropositivity among intravenous drug users. For example, in New York City, the incidence of seropositivity is approximately 60% among intravenous drug users applying for treatment and the incidence of HIV infection in intravenous drug users exceeds the incidence of infection among homosexual males (8). In San Francisco, however, the incidence of seropositivity in a comparable population is only 15% (8).

More than one-third of all AIDS patients develop symptoms consistent with AIDS dementia complex, and one-third of these present with such symptoms at the time the diagnosis of AIDS is first made (67-69). Thus, in the substance abuser with AIDS, the neuropsychiatric manifestations of AIDS dementia complex may complicate diagnosis and treatment because the cognitive, emotional, and behavioral changes that occur in substance abusers with AIDS dementia complex may be

confused with various states of intoxication or withdrawal or a non-AIDS-related affective or psychotic disorder. The course of AIDS-related dementia is variable. Early signs and symptoms may be subtle, but AIDS dementia complex generally progresses to severe global impairment within months. Depression (with suicide as a complication), and psychosis are frequent complications of AIDS dementia complex (70).

THE ROLE OF THE PSYCHIATRIST IN THE TREATMENT OF SUBSTANCE ABUSE DISORDERS

General Principles

Although psychiatrists are ideally suited to provide, direct, coordinate, and monitor psychotherapeutic, pharmacological, and other modalities (71) in the treatment of substance abusers, most clinicians are often skeptical and pessimistic about the efficacy of treatment for these patients. However, with appropriate training and clinical experience, the interested practitioner should be able to achieve considerable success with most patients. Busy practitioners who are not trained or experienced with substance abuse disorders can often successfully work or coordinate their efforts with more intensive treatment programs.

Many different professional and self-help treatments have been developed. The primary challenge is to match patients to the appropriate treatments. The general goals of substance abuse treatment are twofold: to establish abstinence from addicting substances and to promote the individual's physical, psychological, and social well-being. Successful treatment fosters hope, psychological change, and emotional maturation, which, in turn, consolidate recovery, decrease the risk of relapse, and may promote emotional growth beyond the individual's level of premorbid functioning.

Initiating the Treatment Process

The initial goals in the treatment of substance abusers are to make the diagnosis, convey it to the patient and family, and establish a commitment on the part of the patient to achieve abstinence and an understanding of the obstacles in maintaining it. Many patients will argue that their drug and/or alcohol abuse can be moderated and subsequently controlled. Supporting this contention are data from some post hoc studies of alcoholics suggesting that certain patients can achieve a stable recovery with controlled drinking (72, 73). These individuals tend to be persons who have drunk less heavily and have suffered fewer sequelae of the disease (74). In general, however, it is not possible to anticipate which alcoholic can or will return to controlled drinking. As a result, the vast majority of experienced clinicians recommend a commitment to total abstinence for alcoholics (75-78) as well as for other types of substance abusers. The requirement for abstinence is further supported by data from the Treatment Outcome

Prospective Study, which showed a higher relapse rate to the drug of choice (i.e., main drug) when any substance was used (79).

In most patients, detoxification will be followed by a period of variable duration in which withdrawal symptoms will gradually attenuate. Recovery, however, proceeds slowly, often over many years. Neurological sequelae may slowly resolve, psychological and physical trauma resulting from substance abuse may abate, and a newly acquired but fragile state of sobriety may be consolidated. Whether this occurs depends on a host of factors, including patient motivation for change, the presence or absence of family and social supports, the availability and appreciation of appropriate treatment modalities, and the ability of the patient to cope with internal and external cues that trigger drug craving. Additional factors, such as diagnostic groupings (antisocial personality disorder versus primary alcoholism), age at onset of alcoholism, and concurrent drug abuse may also alter the recovery process and sobriety.

Referral for Inpatient Treatment

The choice of treatment or treatments for addicted patients has generally been based on clinical experience, taking into account the type and severity of the addiction, the presence or absence of polydrug use, the presence or absence of associated medical and psychiatric problems, cultural and socioeconomic issues, and the availability of particular treatment resources. The decision to refer an addicted individual for inpatient treatment should obviously be made on a case-by-case basis. In general, such treatment is indicated in the presence of 1) associated major medical and/or psychiatric problems and their actual or imminent complications (liver failure or depression with suicidal ideation, for example), 2) actual or anticipated severe withdrawal, particularly after prolonged heavy use of CNS depressants, 3) multiple failed attempts at outpatient treatment, 4) family, friends, or self-help group members unavailable or unable to provide an adequate social network to support abstinence, and 5) a high degree of chronicity and severe addiction, with polysubstance abuse.

Inpatient treatment may be solely for the purpose of detoxification, followed by a trial of outpatient care. Alternatively, a more extensive (and lengthy) inpatient program should be considered for patients who manifest extensive denial of the problem, are severely addicted, have substantial accompanying physical or mental disorder, including organic impairment, or have quickly relapsed after previous episodes of outpatient or inpatient detoxification. Inpatient treatment may be obtained in freestanding alcohol and drug treatment residential programs or in substance abuse treatment units located in psychiatric or general hospitals. The latter are particularly useful for patients with moderate to severe psychiatric comorbidity.

Preliminary reports have indicated that ambulatory programs using an outpatient day hospital approach can be used safely and more economically to treat mild

to moderate alcohol withdrawal syndromes (80, 81), and Washton (82) has argued for its effectiveness for cocaine-abusing patients. Given the current pressures for cost containment and the preliminary evidence that many (or most, as some [83] would argue) patients do as well in outpatient programs, we will have to remain vigilant about whether future experience and studies support such a contention. Ultimately, the challenge remains for us as psychiatrists to match our patients with the most suitable treatments.

The Rehabilitation Process

General principles. Rehabilitation refers to a treatment process that begins after detoxification is completed. This process may take place in an inpatient or outpatient setting. It often includes individual, group, and family therapy as well as drug and alcohol education and attempts to guide patients and families in developing a social environment that supports abstinence (75). Therapeutic techniques are directed toward helping the patient dismantle maladaptive defenses and learn behaviors conducive to preventing relapse. Treatment staff are typically multidisciplinary in nature, but the emphasis should be on a medical (i.e., disease) model that minimizes stigma and blame.

Most rehabilitation programs have adopted an active psychoeducational program that emphasizes the adverse biological, psychological, and spiritual consequences of persistent and heavy use of substances. Additionally, many programs adopt a didactic approach to instruct patients about factors that lead to relapse. The importance of patient education by the psychiatrist, particularly regarding the medical consequences of heavy drinking, cannot be underestimated. For example, studies directed at diminished drinking, such as the one reported by Chick et al. (84), demonstrated that such education in combination with advice can yield a very positive outcome.

The role of family treatment. A growing literature has served to emphasize the importance of familial factors in the onset and clinical course of both alcoholism and drug abuse (85, 86). Researchers have also delineated several types of families of addicts based on drinking patterns (87), family developmental issues (19), or family functional status (88). These findings have important implications for treatment, and treatment services for families are increasingly viewed as an essential component of a comprehensive substance abuse treatment program.

Familial dysfunction is often circular. Clinical reports note both the role of familial psychopathology in the genesis of addiction and the impact of dysfunctional family behavior that develops in response to chronic drug or alcohol abuse by one or more of its members.

The role of family dynamics in treatment and recovery has been obscured by the myriad treatment approaches used and by the problem of matching index patients and their families to appropriate treatment modalities. The family systems approach attempts to un-

derstand and modify the impact of the family environment on its addicted member or members and the impact of the addict or addicts on the interactions within the family.

In general, effective family treatment assists members in examining how relationships and emotions are processed within the family system. At the same time, it helps the family develop practical ways to become involved in the substance abuser's treatment and recovery. Work with the patient's family should focus on replacing enabling or punitive attitudes and behaviors with more supportive interactions, and spouses or significant others should be direct participants in the therapeutic process (19).

The role of self-help groups. Most psychiatrists understand that self-help groups can be useful in the treatment of substance abusers and patients with other kinds of "addictive" behaviors. Alcoholics Anonymous (AA) currently has more than a million and a half active members worldwide, of whom about 775,000 are in the United States. Emrick (89) has reviewed how AA is effective for participants who remain in the program and attend meetings. The emphasis is on empirical methods for relapse prevention and techniques for promoting psychological growth. AA insists on complete abstinence accomplished one day at a time and reinforced by mutual help and support. Other self-help groups, like Narcotics Anonymous, Gamblers Anonymous, and Overeaters Anonymous, have been modeled after AA and also include regular meetings, sponsorship, and a lengthy process of self- and spiritual development, as characterized by the 12 steps.

Although some clinicians may feel uncomfortable with the language, style, or assumptions of self-help groups, there are substantial data to suggest that these groups work to facilitate recovery. Where conflict develops between self-help adherents and professional systems, patients may be caught in the middle. Patients resisting abstinence may exploit psychodynamically oriented treatment to deny their addiction and justify refusal to explore self-help approaches. Patients already in a self-help group, particularly those who were medically and psychotherapeutically mismanaged, may not trust clinicians to understand and protect their abstinence. How psychiatric interventions can be integrated with such programs is an important area for further research. Self-help programs like AA and Narcotics, Drugs, Cocaine or Pills Anonymous (89) should be explicitly recommended, and any reservations about attendance should be discussed and worked through. Therapists should also attend a sufficient number of self-help group meetings that they are familiar with the supportive, change-producing benefits of such programs.

Psychopharmacological treatment in substance abusers. It is beyond the scope of this paper to review the role of various psychoactive drugs in the treatment of substance use disorders. Suffice it to say that specific pharmacological treatments may play an important role in the treatment of substance abusers. Examples include antidepressants or dopamine agonists to reduce

cocaine craving (60); naltrexone, a narcotic antagonist, in the prevention of relapse of opiate addiction (90); disulfiram in the rehabilitation of alcoholics (91); benzodiazepines in the amelioration of depressant withdrawal (92); clonidine in the treatment of opiate withdrawal (93); and methadone in the detoxification or maintenance treatment of opiate addicts (94).

Measuring Treatment Effectiveness

Although this paper has taken a "proactive" stance regarding the treatment of substance use disorders, it should be mentioned that controversy exists over the effectiveness of such treatment. For example, Vaillant (74), in a "natural history" study, reported that "the results of a treatment were no better than the natural history of the disease," and Edwards et al. (95) suggested that treatment may be no more valuable than a "single session of medical advice." However, such studies have failed to consider the incomparability of treated versus untreated study groups (96) and the role of severity as a factor in treatment outcome.

With respect to the effectiveness of treatment, data from treatment outcome studies suggest that patient characteristics may be more predictive of outcome than the characteristics of the treatment programs themselves (97). Positive treatment outcome in substance abusers has been found to be positively correlated with high socioeconomic stability, the absence of concurrent antisocial personality disorder, a negative family history of alcoholism, and having fewer psychiatric and medical problems.

In psychiatrically symptomatic patients with substance use disorders, Woody et al. (98) have found that patients with the fewest psychiatric symptoms did well in either inpatient or outpatient settings, even when addiction counselors rather than more extensively trained professionals served as primary therapists. In general, outcome is improved when substance-abusing patients are matched to appropriate treatment settings, modalities, and/or clinicians (71). The data from Woody et al. lend support for the efficacy of psychotherapy with appropriately selected addicts.

Finally, modern-day technology permits cost-effective employment of laboratory tests, including testing of urine for illicit drugs, to monitor or evaluate for relapse or use of substances. Holt et al. (99), for example, have shown that a combination of elevated serum glutamyltransferase and erythrocyte mean corpuscular volume identified 90% of alcoholic patients.

BARRIERS TO THE SUCCESSFUL TREATMENT OF SUBSTANCE ABUSE

The Clinician-Patient Interaction

The substance abuser is embedded in a web of psychological distortions, maladaptive behaviors, and neurological deficits that hinder entry into and compliance

with treatment. Denial, projection, minimization, avoidance, omnipotence, and grandiosity must be recognized by the clinician and interpreted to the patient. Unfortunately, accomplishment of this task is frequently thwarted by the fact that substance abusers often elicit negative affect and countertransference reactions in their treaters, which, in turn, result in avoidance or overt rejection of these patients. Unless negative emotions such as anger and contempt are recognized and appropriately dealt with by the clinician, they surface in more subtle forms, including negative judgments about motivation, expressions of disappointment, or stereotypic generalizations about substance abusers as a group. The latter may result in a failure to respond to the unique individual characteristics and needs of each patient and insistence on identical treatment for all substance abusers. Repressed negative emotions may also lead to reaction formation, manifested by inappropriate permissiveness with regard to continued substance abuse. Alternatively, denial and repression of negative affects and attitudes toward the substance-abusing patient may lead to a failure to even recognize the problem.

Training and Clinical Competence in the Treatment of Substance Abusers

Most medical students and residents have not been appropriately trained to deal with the problems of substance abuse. As a consequence, such problems are underrecognized and inadequately treated. The development and dissemination of greater knowledge and skills as well as positive experiences in the treatment of substance abusers can help physicians to overcome barriers to treatment. Competent, experienced clinician-teachers with knowledge of substance abuse and positive experience with treatment are vital to the field. To accomplish this, we need to train a generation of medical practitioners who are competent to diagnose and treat substance use disorders. Recent changes in residency training and the establishment of specialized fellowship programs are promising developments. However, the latter will require adequate federal funding to survive. Moreover, there are still many academic institutions where there are few, if any, medical professionals available to teach or train clinicians in this area. In these instances, consideration should be given to interim measures, including the use of AA members and alcoholism counselors as faculty.

Notwithstanding the difficulties and shortcomings, recent developments that are promising include both required and elective options in the training sequence for psychiatrists. It is now required that substance abuse experience be included during training in postgraduate years 1–4. In addition, APA and the ABPN have proposed the establishment of an optional postgraduate year 5 experience to provide added qualification in addiction psychiatry. Already, 34 residency programs in the United States provide the option for such a fellowship experience (Marc Galanter, personal communication), and the emergence of this

training will assure qualified specialist teachers for substance abuse.

Finally, consideration should be given to refunding the now defunct federal Career Teachers Program in the Addictions, through which 55 (mostly junior) faculty members were given 3-year awards to develop curricula at their respective medical schools. The majority of these faculty continued active careers in teaching about the addictions (100).

CONCLUSIONS

This paper has reviewed some of the recent developments in our understanding of substance use disorders and the role of the psychiatrist-clinician in the evaluation and treatment of patients with these disorders. It has also noted some of the obstacles to full involvement in this field by medical practitioners in general and psychiatrists in particular.

The psychiatrist has a critical role to play in the diagnosis and treatment of patients with substance use disorders. As biopsychosocial phenomena, substance abuse problems constitute a special and direct challenge to the psychiatrist, whose training, perspective, and competence should span all three domains. We must be willing to accept this challenge and fully participate in the development and application of treatment strategies adequate to cope with the enormous human suffering resulting from the abuse of alcohol and other psychoactive drugs.

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Recent Advances in the Phencyclidine Model of Schizophrenia

Daniel C. Javitt, M.D., Ph.D., and Stephen R. Zukin, M.D.

***Objective:** Phencyclidine (PCP, "angel dust") induces a psychotomimetic state that closely resembles schizophrenia. As opposed to amphetamine-induced psychosis, PCP-induced psychosis incorporates both positive (e.g., hallucinations, paranoia) and negative (e.g., emotional withdrawal, motor retardation) schizophrenic symptoms. PCP-induced psychosis also uniquely incorporates the formal thought disorder and neuropsychological deficits associated with schizophrenia. The purpose of the present paper is to review recent advances in the study of the molecular mechanisms of PCP action and to describe their implications for the understanding of schizophrenic pathophysiology. **Method:** Twenty-five papers were identified that described the clinical dose and serum and CSF levels at which PCP induces its psychotomimetic effects. The dose range of PCP-induced effects were compared to the dose range at which PCP interacts with specific molecular targets and affects neurotransmission. **Results:** It was found that PCP-induced psychotomimetic effects are associated with submicromolar serum concentrations of PCP. At these concentrations PCP interacts selectively with a specific binding site (PCP receptor) that is associated with the N-methyl-D-aspartate (NMDA)-type excitatory amino acid receptor. Occupation of its receptor by PCP induces noncompetitive inhibition of NMDA receptor-mediated neurotransmission. Other NMDA antagonists such as the dissociative anesthetic ketamine induce PCP-like neurobehavioral effects in proportion to their potency in binding to the PCP receptor and inducing NMDA receptor inhibition. **Conclusions:** These findings suggest that endogenous dysfunction of NMDA receptor-mediated neurotransmission might contribute to the pathogenesis of schizophrenia. The relative implications of the PCP and amphetamine models of schizophrenia are discussed in relationship to the diagnosis and etiology of schizophrenia.*

(Am J Psychiatry 1991; 148:1301-1308)

Analysis of drug-induced model psychoses has been one of the most effective approaches for investigating neurochemical abnormalities associated with schizophrenia. The most widely studied neurochemical hypothesis of schizophrenia, the dopamine hypothesis, derives in large part from the observation that amphetamine can induce symptoms resembling those of acute paranoid schizophrenia by augmenting dopaminergic neurotransmission within the CNS (1). However, many schizophrenic patients fail to respond ade-

quately to treatment with dopamine antagonists, suggesting that the amphetamine model fails to account for important dimensions of the illness.

An alternative model of schizophrenia based upon the psychotomimetic effects of phencyclidine (PCP, "angel dust") was first proposed over 25 years ago (2). At that time the neurochemical actions of PCP were poorly understood. Research over the past decade, however, has revealed unique mechanisms by which PCP induces its behavioral effects at the neuroreceptor level. These advances permit the development of new hypotheses concerning neurochemical dysfunction in schizophrenia and may permit new treatment strategies for patients whose symptoms conform poorly to the predictions of the amphetamine model of schizophrenia.

CLINICAL STUDIES

PCP-Induced Psychosis

PCP was developed as a general anesthetic in the late 1950s (3-5). In initial clinical trials, PCP uniquely induced a catatonia-like state that permitted performance

Presented at the 142nd annual meeting of the American Psychiatric Association, San Francisco, May 6-11, 1989. Received July 25, 1990; revision received Feb. 20, 1991; accepted March 9, 1991. From the Departments of Psychiatry and Neuroscience, Albert Einstein College of Medicine/Montefiore Medical Center and Bronx Psychiatric Center, Bronx, N.Y. Address reprint requests to Dr. Javitt, Department of Psychiatry, Forchheimer Building, Rm. 101, Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461.

Supported in part by National Institute on Drug Abuse grant DA-03383 (Dr. Zukin) and NIMH grant MH-00631 (Dr. Javitt), the Ritter Foundation (Dr. Zukin), a Young Investigator Award from the National Alliance for Research on Schizophrenia and Depression (Dr. Javitt), and the Department of Psychiatry, Albert Einstein College of Medicine/Montefiore Medical Center.

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of minor surgical procedures but which differed markedly from the state of relaxed sleep induced by barbiturate or opiate anesthetics (3–5). During PCP-induced anesthesia, patients manifested a flat expression and a complete loss of expression, with open mouth and fixed, sightless staring (3). They became generally rigid and at times developed waxy flexibility similar to that seen in endogenous catatonic states and akinetic mutism (3). The overall behavioral state was one of evident and marked dissociation from the environment without complete loss of consciousness (3–5). The PCP derivatives cyclohexamine (3) and ketamine (6) were subsequently found to induce dissociated, catatonia-like states similar to that induced by the parent compound. These compounds were thus collectively described as “dissociative anesthetics” (6).

Up to 50% of patients given PCP anesthesia developed severe intraoperative reactions characterized by agitation and hallucinations (3–5). In a large percentage of these subjects, PCP-induced psychotic reactions, including excitation, bizarre behavior, paranoia, concreteness of thought, and severe hallucinatory disturbances, persisted beyond emergence from anesthesia. Drug-emergent psychotic states typically lasted for 12 to 72 hours following anesthesia but occasionally persisted for up to 7–10 days (4; 7). Similar effects were observed when PCP was tried as an oral analgesic agent, at subanesthetic doses, for control of chronic pain (7). These striking findings prompted a series of studies on the effects of subanesthetic doses of PCP in normal volunteers and schizophrenic subjects that continued until the drug was withdrawn from clinical use in 1965.

Psychotomimetic Effects of PCP in Normal Volunteers

In normal volunteers, subanesthetic doses (0.05–0.1 mg/kg i.v.) of PCP produced acute psychotic reactions of several hours' duration (8–13). Subjects became progressively withdrawn, autistic, and negativistic, in some cases to the point of catatonic posturing and perseveration (8). Subjects lost the ability to maintain a cognitive set. Proverb interpretation and responses to projective testing became concrete, impoverished, idiosyncratic, and bizarre and were accompanied by general poverty of speech and thought (8–13). The overall behavioral state and quality of the thought disorder induced by PCP was felt by investigators to be highly reminiscent of an acute schizophrenic decompensation (8–13).

In formal studies of neuropsychological functioning, PCP induced a spectrum of disturbances in attention (14), perception (11, 14), and symbolic thinking (11, 15) uniquely similar to that observed in schizophrenia (14, 15). LSD, amobarbital, and amphetamine failed to induce similar neuropsychological disturbances (14, 15). Tests that required selective attention and paired-associate learning were most affected by low-dose PCP administration (8), suggesting that, as in schizophrenia

(16, 17), frontal lobe and temporohippocampal processing is most severely disturbed.

Effects of PCP in Schizophrenic Subjects

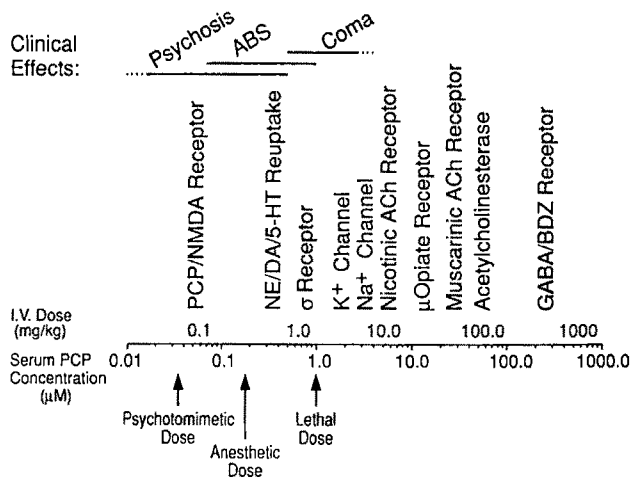
Administration of PCP to schizophrenic subjects led to exacerbation of thought disorder and increased assertiveness and hostility (9, 10, 12, 18). In stabilized schizophrenic subjects, single low doses of PCP led to rekindling of presenting symptoms that lasted for days (10) to weeks (9, 12). Body image disturbances, depersonalization, estrangement, thought disorder, and inappropriate affect were evoked or worsened (9, 10, 12, 18). By contrast to LSD, which was felt to induce symptoms that resembled secondary characteristics of schizophrenia, PCP was reported to rekindle primary, “pathology-specific” perceptual and cognitive abnormalities (9, 12). Only patients who had previously undergone prefrontal lobotomies proved relatively resistant to the psychotomimetic effects of PCP (18).

Chronic, stabilized schizophrenic subjects are generally hyporesponsive to the effects of amphetamine (19) and may show paradoxical behavioral improvement (20). The ability of PCP to exacerbate psychotic symptoms in chronic as well as acute schizophrenic subjects therefore distinguishes it from amphetamine and suggests that the neural substrates affected by PCP are vulnerable in subjects with the schizophrenic trait, while the neural substrates affected by amphetamine are vulnerable only in subjects in the acutely decompensated state.

PCP Abuse

Further characterization of the psychotomimetic actions of PCP was facilitated by the epidemic of PCP abuse that occurred during the late 1960s and 1970s. Low-dose intoxication (5–10 mg orally, by insufflation or by inhalation) was reported to induce agitation, excitement, catalepsy, and mutism (21). Hallucinations, delusions, paranoia, thought disorder, and catatonia without clouding of consciousness were found to persist in some PCP abusers for days to weeks after single ingestions (21–24). In retrospective studies it was determined that PCP-intoxicated patients could not be distinguished from schizophrenic patients on the basis of presenting symptoms alone (25, 26).

The proportion of patients who developed a psychotic state after acute administration of PCP is difficult to estimate from retrospective clinical studies. In one such study, 25% of PCP-intoxicated patients who presented on an army base required psychiatric admission (22). Similarly, a study of 1,000 patients who presented with acute PCP intoxication found that 30% presented with catatonic or psychotic reactions and an additional 25% manifested bizarre, violent, or agitated behavior. Further, of those patients who presented in an acute PCP-induced stuporous or comatose state, approximately 25% developed catatonic or psychotic reactions after resolution of the acute brain syndrome (24). The percentage of patients who manifest psychotic reactions

FIGURE 1. Dose Range of PCP Effects^a

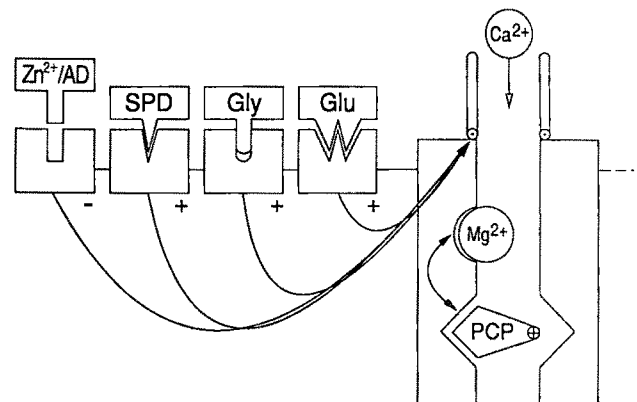
^aShaded area represents range of clinically relevant interactions.

following exposure to PCP compares favorably with the 0%–19% rate of psychosis in nonschizophrenic subjects after acute exposure to amphetamine or methylphenidate (27).

MOLECULAR MECHANISMS OF PCP ACTION

PCP is a lipid-soluble molecule that crosses the blood-brain barrier readily following peripheral administration. On the basis of pharmacokinetic considerations (28), it can be calculated that a low psychotomimetic dose of 0.1 mg/kg i.v. would produce a serum PCP concentration of 0.01–0.10 μM , as would a single 5-mg “street” dose (i.e., one pill, “joint,” or “line”) (21) of PCP. These calculations are consistent with the observation that PCP-induced psychosis is selectively associated with serum PCP concentrations that range from undetectable (less than 0.02 μM) to 0.40 μM (100 ng/ml) in patients who present with acute PCP-intoxication (29, 30). Concentrations above 0.40 μM (100 ng/ml) are almost invariably associated with gross impairment of consciousness, while concentrations above 1.0 μM (250 ng/ml) are associated with coma, seizures, and respiratory arrest (29, 30). The highest recorded serum and CSF concentrations are in the range of 1.0–2.0 μM (250–500 ng/ml) (29–34).

Over the past 25 years, considerable effort has been devoted to identifying the site at which PCP mediates its psychotomimetic effects. Given the dose range of PCP effects, a molecular target site mediating PCP psychosis must have submicromolar affinity for PCP. A candidate site must also show appropriate affinity for other drugs, such as ketamine, which exert PCP-like behavioral effects clinically. Although PCP has been reported to interact with a large number of molecular target sites (figure 1), the majority of these interactions occur at concentrations that are unlikely to be reached in clinical situations (35–39).

FIGURE 2. Schematic Model of NMDA Receptor Functioning^a

^aZn²⁺=zinc, AD=tricyclic antidepressants, SPD=spermidine, GLY=glycine, GLU=L-glutamate, Mg²⁺=magnesium, and Ca²⁺=calcium.

A binding site with submicromolar affinity for PCP was first demonstrated in 1979 (40, 41). The dissociative anesthetics cyclohexamine and ketamine, the “designer drugs” 1-[1-(2-thienyl)cyclohexyl]piperidine, *N*-ethyl-1-phenylcyclohexylamine, and 1-(1-phenylcyclohexyl)pyrrolidine and, more recently, the novel anti-ischemic agent MK-801 (42–44) were all found to interact with the PCP receptor at doses appropriate to their neurobehavioral effects. By contrast, a wide variety of dopaminergic, serotonergic, and GABA-ergic agents were found not to interact with the PCP receptor at physiological concentrations (40–44).

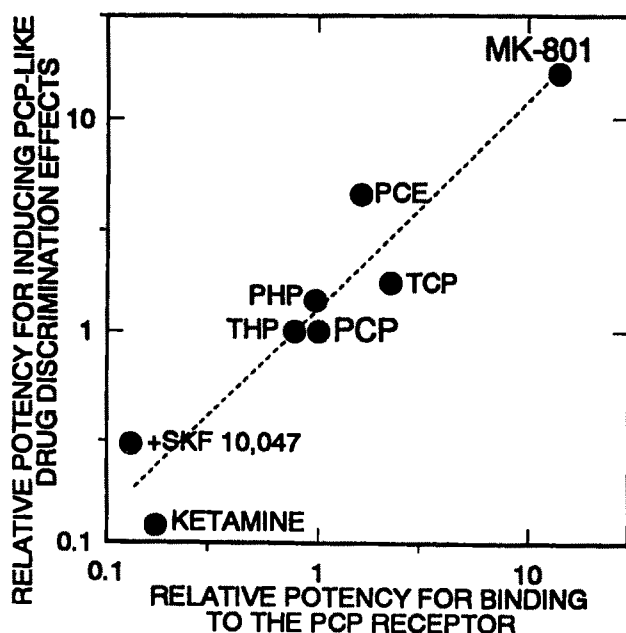
Studies since 1979 have established that the PCP receptor represents a site located within the ion channel formed by the *N*-methyl-D-aspartate (NMDA) receptor complex (figure 2). NMDA receptors are a type of receptor for the excitatory amino acid neurotransmitter L-glutamate, the major excitatory neurotransmitter in the brain (45). PCP inhibits NMDA receptor-mediated neurotransmitter release half-maximally, 0.07–0.08 (42, 46) μM , identical to its affinity for the PCP receptor. Agents that bind to the PCP receptor thus inhibit the normal functioning of the NMDA receptor complex, leading to disturbances of NMDA receptor-mediated glutamatergic neurotransmission. Since PCP binds to a site on the NMDA receptor complex that is distinct from the recognition site for the neurotransmitter glutamate, its inhibitory effects are noncompetitive in that they cannot be overcome by increased neurotransmitter concentrations.

PCP-INDUCED BEHAVIORS

Drug Discrimination

The role of the PCP/NMDA receptor complex in mediating the neurobehavioral effects of PCP and other dissociative anesthetics is supported by drug dis-

FIGURE 3. Scatter Plot of the Correlation Between the Potency of Psychoactive Agents in Inducing PCP-Like Behavioral Effects in the Drug Discrimination Paradigm (47–49) and Their Potency in Binding to the PCP Receptor (40–44)^a



^aSee text for abbreviations.

crimination studies. In such studies, animals are trained to respond differentially to peripheral injection of either a reference drug or placebo. Once animals have learned to recognize the subjective (introceptive) cue provided by the reference drug, novel agents are tested to determine whether they induce drug-appropriate responses. Agents that induce similar introceptive cues in animals usually share a large number of other pharmacological properties and produce similar subjective effects in man (46).

Using the drug discrimination paradigm, researchers have demonstrated that PCP-appropriate responses can be induced by 1-[1-(2-thienyl)cyclohexyl]piperidine, N-ethyl-1-phenylcyclohexylamine, ketamine (47, 48) and MK-801 (49). The potencies with which these and other agents induce PCP-like discriminative stimulus effects correspond to their potencies in binding to the NMDA receptor-associated PCP receptor (figure 3), suggesting that the discriminative stimulus effects of PCP reflect its action at PCP receptors.

PCP-appropriate responses are not inhibited by dopamine antagonists such as haloperidol and are not reproduced by dopamine agonists such as amphetamine or methylphenidate (47). A wide variety of serotonergic, adrenergic, GABA-ergic, and opiate agents similarly fail to induce or antagonize PCP-like discriminative stimulus effects (47). The dose at which PCP induces half-maximal discriminative stimulus effects in monkeys, 0.1–0.2 mg/kg (47, 48), is similar to the dose at which it induces psychotomimetic effects clinically.

Unconditioned Behaviors

In mice and rats, PCP induces a characteristic syndrome of hyperactivity and stereotypies that partially resemble those induced by dopaminergic agents such as amphetamine or methylphenidate (50–52). At doses approximately 10-fold greater than those at which it binds to the PCP receptor, PCP inhibits dopamine reuptake by binding to the neuronal monoamine reuptake pump (50, 53). It has therefore been proposed that PCP-induced hyperactivity and stereotypies, and by extension PCP-induced psychotomimetic effects, might result from direct inhibition of dopamine reuptake (50). However, drugs such as MK-801 that bind with high potency to the PCP receptor but do not affect dopamine reuptake reproduce the full range of PCP-induced behaviors (54). By contrast, PCP derivatives that block dopamine reuptake but do not bind to the PCP receptor fail to fully reproduce the PCP-induced behavioral syndrome (54). Finally, PCP-like behavioral effects can be induced even in monoamine-depleted mice (53), suggesting that dopaminergic dysregulation is not required for their expression.

PCP Receptor-Mediated Dysregulation of Dopaminergic Neurotransmission

An alternative explanation for the ability of PCP to induce dopamine-like behaviors in rats and mice without primarily altering dopamine release relates to the behaviorally antagonistic interaction between glutamatergic and dopaminergic systems in subcortical structures (55, 56) (figure 4). In striatum and nucleus accumbens, dopamine, acting at D₂ receptors located on cholinergic and GABA-ergic neurons, serves to inhibit GABA-ergic outflow (55, 56), which is itself inhibitory on downstream motor centers (57). Amphetamine, which increases dopamine release, therefore decreases GABA-ergic outflow, leading to behavioral disinhibition. L-Glutamate, acting primarily at NMDA receptors, stimulates GABA-ergic outflow (58) so that inhibition of NMDA receptors also decreases GABA-ergic outflow (58), leading to behavioral disinhibition similar to that seen after amphetamine administration (59, 60). The ability of NMDA and dopamine receptors to exert independent and complementary control over striatal GABA-ergic outflow may also account for the supra-additive nature of the interaction between PCP and amphetamine.

PCP-Induced Tranquilization

In many species other than mice and rats, including guinea pigs, rabbits, cats, dogs, and monkeys, PCP induces a unique syndrome of tranquilization and "calming" such that animals do not respond to handling with their characteristic aggressiveness (61). In monkeys, the tranquilizing effects of PCP are so pronounced that investigators may place their fingers within the animals' mouths with impunity (62). The degree to which PCP

induces tranquilization as compared to hyperactivity appears to depend upon species and behavioral state (61). The selective PCP receptor ligand MK-801 induces tranquilization similar to that induced by PCP (54), suggesting that tranquilization is mediated at the PCP receptor and reflects inhibition of NMDA receptor-mediated neurotransmission.

At present, the neural localization of NMDA receptors involved in the generation of tranquilization has not been established. However, the similarity of monkey tranquilization to PCP-induced catatonia and dissociation supports the contention that the clinical effects of PCP are mediated primarily at the NMDA receptor-associated PCP receptor. The behavioral similarity of tranquilization to the volitional disturbances and catatonia associated with schizophrenia also suggests that PCP psychosis may provide a unique model for negative schizophrenic symptoms.

Effects on Learning and Memory

The cognitive effects of PCP are a final category of behavior that has been investigated using animal models. At concentrations similar to those at which it induces its discriminative stimulus effects, PCP inhibits spatial learning in rats (63, 64) and cats (64) and paired associate learning in monkeys (65, 66). Effects of PCP on learning are reproduced by ketamine (65), MK-801 (67), and other PCP receptor ligands (68) but not by amphetamine (66), suggesting that they are mediated at PCP receptors and are not dependent upon dopaminergic dysregulation. PCP-induced cognitive deficits, like other categories of PCP-induced psychotomimetic effects, thus appear to be due to inhibition of NMDA receptor-mediated neurotransmission.

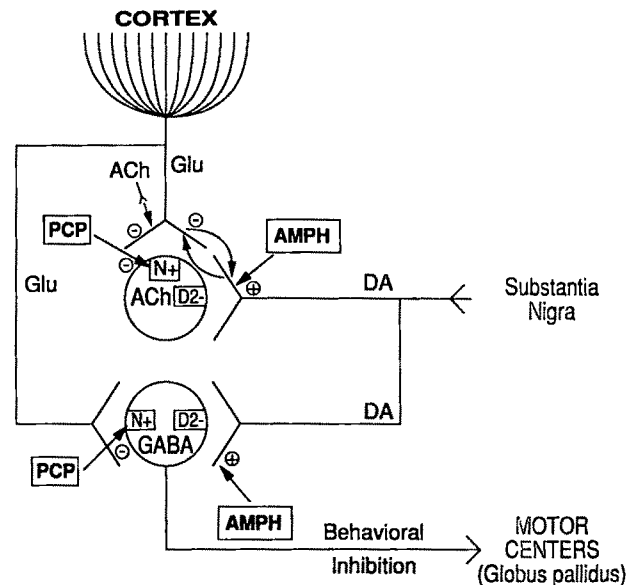
IMPLICATIONS FOR SCHIZOPHRENIA

The ability of PCP to induce schizophreniform psychosis by inhibiting NMDA receptor-mediated neurotransmission suggests that endogenous dysfunction or dysregulation of NMDA receptor-mediated transmission might occur in schizophrenia and contribute to symptom generation. PCP-induced psychosis thus provides a neurochemical hypothesis of schizophrenia distinct from the dopamine hypothesis.

Syndromal Implications

Both amphetamine and PCP induce psychoses that fall within the broad nosological category of schizophrenia. The relative prominence of symptoms induced by these two agents differs considerably. In nonschizophrenic subjects, amphetamine induces positive (69, 70) schizophrenic symptoms such as hostility, agitation, paranoia, and paranoid delusions (71–73) but does not induce such core symptoms as looseness of association, loss of ego boundaries, concreteness, and bizarre associations (71–73). Amphetamine psychosis

FIGURE 4. Schematic Illustration of the Functionally Antagonistic Interaction Between Descending Glutamatergic Pathways and Ascending Dopaminergic Pathways in Striatum^a



^aACh=acetylcholine, GLU=L-glutamate, N=NMDA receptors, AMPH=amphetamine, DA=dopamine. Adapted from reference 55.

thus corresponds to a Schneiderian model of schizophrenia (74) in which it is postulated that specific positive symptoms are fundamental to schizophrenia. However, it has been suggested that both amphetamine psychosis (75) and the Schneiderian model (76) apply to positive psychoses in general and not specifically to schizophrenia. The inability of amphetamine to induce core schizophrenic thought disorder suggests that dopaminergic hyperactivity may play only a limited role in the generation of non-Schneiderian symptoms.

PCP psychosis provides an alternative conceptualization of schizophrenia. Although hallucinations, agitation, paranoia, and paranoid delusions occur after PCP administration, the most striking and consistent behavioral effects of PCP are alterations in body image, disorganization of thought, negativism, and apathy (8–13). The symptoms induced by PCP are thus similar to the “four A’s” proposed by Bleuler to represent the primary symptoms of schizophrenia: affective blunting, ambivalence, autism, and disturbance of association (77). PCP psychosis thus may provide a neurochemical model corresponding uniquely to the Bleulerian conception of schizophrenia.

“Frontal-Lobe” Dysfunction

As noted earlier, a second difference between PCP and amphetamine is their relative ability to induce schizophrenia-like cognitive and neuropsychological deficits. Several large-scale studies of schizophrenia suggest that cognitive deficits and neuropsychological dysfunction form a cluster that is distinct from either positive or negative symptom clusters (78–80) and

that cognitive symptoms are specifically associated with the poor outcome (80). Although it has been proposed that cognitive dysfunction in schizophrenia might result from underlying structural brain damage (81), the ability of PCP to induce reversible, schizophrenia-like neuropsychological abnormalities suggests that a discrete neurochemical deficit could also potentially account for the entire range of symptoms that occur in schizophrenia.

One potential usefulness of the PCP model is its ability to reconcile apparently contradictory aspects of the dopamine hypothesis. Thus, positive schizophrenic symptoms are seen following amphetamine intoxication (71–73) and are suggestive of dopaminergic hyperactivity. Conversely, the “frontal lobe” dysfunction seen in schizophrenia, such as increased perseveration on the Wisconsin Card Sort, may be seen as well in Parkinson’s disease (82) and is correlated with decreased HVA levels (83). Such symptoms are therefore suggestive of dopaminergic underactivity. Thus, no unitary deficit in dopaminergic functioning can account for the spectrum of symptoms seen in schizophrenia. By contrast, primary dysfunction of NMDA receptor functioning could potentially account for the deficit in cognitive functioning associated with schizophrenia, as well as for the dopaminergic hyperactivity and dysregulation associated with acute schizophrenia. A primary dysfunction of NMDA receptors leading to secondary dopaminergic dysregulation would also account for the paucity of neuropathological correlates of the postulated hyperdopaminergic state in schizophrenia (84).

Etiological Implications

At present, the mechanism by which NMDA receptor dysfunction might occur in schizophrenia remains to be determined. In addition to glutamate, NMDA receptors (figure 2) are sensitive to the effects of glycine, polyamines, and specific divalent cations (e.g., Zn^{2+} , Mg^{2+}) (reviewed in reference 45). Abnormal concentrations of glutamate or of any of these factors could therefore potentially lead to decreased NMDA receptor activation. Alternatively, NMDA receptors themselves could be dysfunctional, as has recently been suggested to occur in Alzheimer’s disease (85). Endogenous peptides have been described (86, 87) that have PCP-like neurochemical properties (87) and that therefore may act as endogenous psychotogens. Finally, NMDA receptor-bearing cells are at increased risk for degeneration as a result of excitotoxins or hypoxic/ischemic insults both perinatally and during adulthood (reviewed in reference 45). Degeneration of striatal NMDA receptor-bearing neurons as the result of excitotoxin accumulation has been hypothesized to contribute to the pathophysiology of Huntington’s disease (88), which may present initially with psychotic symptoms. Which, if any, of these mechanisms are operative in schizophrenia remains to be determined. Nevertheless, the ability of PCP to induce a schizophrenia-like psychotic state suggests that investigation into NMDA receptor func-

tioning may lead to insights into the pathophysiology and treatment of schizophrenia.

Future Directions

The value of the PCP model of schizophrenia will ultimately depend upon the degree to which it can account for specific signs of neurophysiological dysfunction in schizophrenia and the degree to which new treatment strategies based upon the PCP model prove therapeutically beneficial. Among the most consistent indices of brain dysfunction in schizophrenia are impaired generation of cognitive event-related potentials (e.g., P300) (89) and decreased prefrontal metabolism (16, 83, 90, 91). Such abnormalities are neither induced nor ameliorated by neuroleptic medication (91, 92), suggesting that they are poorly accounted for by the dopamine model of schizophrenia. Preliminary data suggest that some schizophrenia-like event-related potential abnormalities may be induced by PCP-like agents (93) and that PCP-intoxicated subjects may show prefrontal hypometabolism similar to that observed in schizophrenia (J.C. Wu, M.S. Buchsbaum, and W.E. Bunney, personal communication, 1991). Studies aimed at determining whether PCP-like agents reproduce other signs of brain dysfunction associated with schizophrenia would provide a further test of the PCP model.

NMDA receptor-mediated neurotransmission can be potentiated by agents acting at either the glycine- or polyamine-regulatory sites (figure 2). Preliminary studies suggest that some schizophrenic subjects benefit from treatment with large oral doses of glycine (94). However, glycine penetrates poorly across the blood-brain barrier, and its beneficial effects have been inconsistent (95). Development of centrally active agents capable of stimulating either the glycine or polyamine sites will be crucial for determining whether augmentation of NMDA receptor-mediated neurotransmission will provide a therapeutically valuable approach for the treatment of schizophrenia.

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The Pharmacology of Stuttering: A Critical Review

John Paul Brady, M.D.

***Objective:** The author critically examines the limited world literature on pharmacologic treatments of stuttering. **Method:** The literature on stuttering and drugs was identified by means of two computer-assisted searches. **Findings:** A great variety of pharmacologic agents have been used to treat stuttering, reflecting the many theories about the origin and nature of the disorder. In some instances new hypotheses about the nature of stuttering have followed the chance discovery of agents having some efficacy. **Conclusions:** Few studies have used adequate experimental designs. Promising avenues of research, both for the treatment of stuttering and for exploring its nature, include the use of calcium channel blocking agents and cholinergic drugs.*

(Am J Psychiatry 1991; 148:1309–1316)

Stuttering is easier to recognize than to define precisely. The concise definition provided in *DSM-III-R* will suffice here: "Frequent repetitions or prolongations of sounds or syllables that markedly impair the fluency of speech" (p. 88). It should be noted, however, that in addition to these primary symptoms there are secondary symptoms, which largely represent the efforts of the patient not to stutter. They include blocks or interruptions in the flow of speech sounds, tremors of the lips and jaw, rapid blinking, jerking movements of the head, arm, or upper trunk, and other manifestations of the stutterer's struggle to "get the next word out." These aspects of stuttering are often more distressing to the patient and more striking to the observer than the repetitions and prolongations themselves.

Common or developmental stuttering almost always begins in childhood or early adolescence, it is appreciably more common in males than females at all ages, and it is found in all cultures, races, languages, and historical periods with approximately the same frequency. The prevalence of this kind of stuttering is about 1% of the adult population (1).

Distinct from developmental stuttering is the rarer disorder of neurogenic or "acquired" stuttering. Typically, it has a sudden onset in adults and is almost always associated with gross impairment of brain function such as may result from head trauma, a stroke, a brain tumor, or other insult to the brain (2). Occasionally, it occurs as a side effect of centrally acting drugs, especially neuroleptics (3). Neurogenic stuttering can be distinguished from developmental stuttering on

clinical grounds (4). For example, if a patient with developmental stuttering is asked to read the same sentence repeatedly, his dysfluency will generally decrease with each reading. He may be totally fluent on the 10th or 15th rendition. This phenomenon, termed "the adaptation effect," is generally not seen in neurogenic stuttering. Treatment of neurogenic stuttering is directed first at the underlying source of brain dysfunction, followed by current speech therapy procedures (5); it will not be considered further here. A stuttering-like condition is sometimes seen with use of antidepressant medications. However, this impediment is largely one of speech blockage. The patient has difficulty in word finding rather than in phonation (6–10). It resolves when the offending antidepressant is discontinued or the dosage is reduced.

NONPHARMACOLOGIC TREATMENTS

Few disorders of human beings have been subject to as great a variety of treatments as stuttering. Generally, these have mirrored the theories to explain the condition that were prevalent at the time (11). Hippocrates attributed stuttering to dryness of the tongue and recommended producing varices of the tongue by chemical or surgical means (12). In contrast, the distinguished sixteenth-century Italian physician Hieronymus Mercurialis held that stuttering was due to a "moist and cold" state of the vocal apparatus and recommended cauteries and blisters on the neck and behind the ears in order to desiccate the head (12). Surgical procedures on the tongue, frenulum, or uvula—sometimes quite mutilating—were popular during the nineteenth century. They were based on the assumption that the fault lay in the anatomy of the oral cavity (12).

Psychosocial and behavioral treatments have been as

Received Aug. 20, 1990; revision received Jan. 9, 1991; accepted Feb. 4, 1991. From the Department of Psychiatry, University of Pennsylvania. Address reprint requests to Dr. Brady, 1111 Gates Pavilion, Hospital of the University of Pennsylvania, Philadelphia, PA 19104. Copyright © 1991 American Psychiatric Association.

varied, ranging from operant reinforcement models (reinforce fluency and extinguish or punish dysfluency) to psychoanalytic psychotherapy. The latter, popular during the 1950s and 1960s, was based on the thesis that stuttering is an expression of unconscious conflicts, involving, especially, anal-sadistic wishes (13). In recent years well-designed studies have found stutterers as a group to be remarkably similar to nonstutterers in personality traits and general level of adjustment (14). It is remarkable how well adjusted even most severe stutterers are, given the nearly constant anguish and stress many experience in daily efforts to communicate. Of course, some stutterers have adjustment problems as a consequence of their speech impediment and may benefit from psychotherapy. However, it is very unlikely that stuttering is primarily a psychogenic disorder. Experimental studies over the last two decades point to a developmental disorder of the CNS, possibly derived from subtle abnormalities of central auditory functioning or sensory-motor processing (1). Differences between stutterers and nonstutterers in functional asymmetries of the cerebral hemispheres identified by electrophysiological procedures (e.g., averaged evoked responses) are suggestive of this explanation (15).

Speech pathologists now emphasize treatment approaches that focus on the reshaping of speech sounds, often guided by behavior modification principles (16, 17). It usually requires great vigilance and extended practice to compensate for faulty coordination of respiration, phonation, and articulation. However, many adults with severe stuttering make limited progress despite the faithful application of these retraining principles.

It is surprising that the pharmacologic literature on stuttering is so scant, given the prevalence of the disorder, the distress it causes, and the limited efficacy of nonpharmacologic treatments. With the accumulating evidence that the disorder has its basis in CNS dysregulation, there may be more interest in pharmacologic approaches in the future.

EARLY DRUG STUDIES

It is convenient to review first the reports published before the modern era of psychopharmacology (about the mid-1950s). Since stuttering is a behavior that is very sensitive to suggestion and placebo effects as well as observer bias, two essentials of treatment trials in this disorder are experimental controls and objective, quantitative measures of fluency. Because most of these early reports lack both, they will be described only briefly.

Carbon Dioxide

Meduna reintroduced carbon dioxide therapy into psychiatry in the late 1940s (18–20). His procedure consisted of 25 or so inhalations of a mixture of 30% carbon dioxide and 70% oxygen. This usually results

in loss of consciousness followed by a period of psychomotor excitement. Typically, patients were given two or three treatments per week for a total of 100–150 treatments. Meduna applied the procedure to a variety of psychoneurotic conditions, including conversion disorders, phobic disorders, dissociative states, and stuttering. He hypothesized that these conditions are characterized by abnormally low thresholds for stimulation and that carbon dioxide normalized these thresholds (20).

Early reports of the efficacy of this treatment with stutterers stimulated many others to use the procedure (21–26). Ingham (27) has chronicled the amazing growth and then decline of enthusiasm for this treatment of stuttering. In brief, treatment results were reported only in vague terms without actual speech data, and there was no reported evidence of improved fluency extending beyond the acute treatment period. The only controlled study, carried out by Arthurs et al. in 1954 (28), showed no differences in outcome between subjects who were given carbon dioxide therapy and those who were given inhalations of nitrous oxide, a presumed active placebo.

Since there have been no published reports of this treatment for stuttering in almost 30 years, one can assume that its lack of efficacy is now accepted. Aside from the occasional use of carbon dioxide/oxygen mixtures as an adjunct to desensitization procedures in behavior therapy for anxiety disorders (29, 30), this treatment is no longer used in psychiatry.

Stimulants

In the early literature, no clear rationale was given for using stimulants in the treatment of stuttering. Tuttle (31) described the case of a 24-year-old woman he treated for anxiety neurosis who had frequent episodes of hyperventilation. She had a chronic severe stutter as well. He conducted one therapeutic interview after injecting 12.5 mg of methamphetamine, which he reported had some beneficial effect on her hyperventilation syndrome. Remarkable, however, was the dramatic reduction in her stuttering during this one session. Apparently, the single treatment had no lasting beneficial effect. Cerciello (32) reported treating several stutterers with amphetamine and finding it helpful, especially when combined with orthophonic (speech) therapy and psychotherapy. Fish and Bowling (33) reported similar results in another uncontrolled study without objective speech data.

Sedatives

Whether anxiety plays a primary etiological role in stuttering or not, it no doubt often aggravates dysfluency in particular situations. Hence, sedative medications have often been tried. In 1940 Hogewind (34) reported the use of Bellergal, a medication still in use for "functional disorders," which consists of phenobarbital, ergotamine tartrate, and alkaloids of belladonna.

The predominant effect is sedation. Again, no details of speech were given; the author simply stated that the results were "satisfactory, sometimes very good." Yannatos (35) reported using hydroxyzine, an antihistaminic drug used today mainly for the symptomatic treatment of allergic dermatoses. It has sedative and anxiolytic properties as well. He claimed good results with 42 stutterers who received speech therapy also. He found little value in using hydroxyzine alone.

Derazne (36) published an intriguing report from Russia in 1966. He treated "a few thousand children" with bromides and calcium chloride. Bromides were introduced into medicine during the last century as sedatives and anticonvulsants. They were largely abandoned several decades ago when more effective and safer sedatives and anticonvulsants were developed. Apparently, Derazne administered the drugs several times a day in large (but unstated) doses for a 2- to 3-month period. He stressed that the children slept "at least 13 hours a day." The calcium chloride was probably added to minimize the extensive substitution of bromide ions for chloride ions, which accounts for some of the unwanted side effects of bromide therapy. The lengthy sleep of the children was probably bromide-induced, and this therapy really represented a form of "sleep therapy," which was once very common in the Soviet Union for a variety of psychiatric disorders. In any case, the author gave few detailed clinical data but implied that most of the children were cured of their speech impediments.

In one of the first studies that used speech data and some experimental control, Love (37) reported on 20 stutterers treated under four conditions: no drug, a placebo, a stimulant (amphetamine), and a sedative (pentobarbital). No differences in the results of the treatments were found.

Other Drugs

Two reports in the 1950s (38, 39) claimed good results with glutamic acid, an amino acid widely distributed in the CNS, where it is a potent excitatory neurotransmitter. Neither report gave sufficient detail to evaluate the efficacy of the treatment, and neither gave a clear rationale for its use in stuttering. More recently, Rastatter and Harr (40) reported an intensive biochemical investigation of five stutterers in which they measured plasma levels of adrenergic neurotransmitters and several primary amino acids. The one abnormality they found was that the stutterers had glutamine levels which were more than 4 standard deviations higher than the reference mean (about 540 mol/liter). These authors argued, by a rather circuitous route, that this might reflect the disturbed interhemispheric interactions which many investigators have implicated in dysfluent speech. Unfortunately, they relied on a "reference mean" for comparison rather than establishing a standard in their own laboratory with control (nonstuttering) subjects. In any event, it is difficult to relate Rastatter and Harr's ex-

perimental finding of an excess of glutamine in stutterers to the therapeutic value of glutamic acid supplements in this disorder.

In 1951 Hale (41) reported using thiamine supplements to arrest the development of stuttering in preschool children who showed early signs of the disorder. He hypothesized that undetected and otherwise asymptomatic deficiencies of this vitamin might induce hypertonicity of muscle and, hence, disrupted speech in susceptible children. His study, which used a crossover experimental design, was double-blind and placebo-controlled. Important details were lacking, however. No speech data were offered, the number of subjects was not given, and differences between the drug and placebo were not clearly stated, although the author implied that thiamine was proved to be effective. Penson (42) later completed a trial of thiamine in adult stutterers and found little evidence of benefit.

Reserpine, derived from the root of the Indian plant *Rauwolfia serpentina*, was introduced into psychiatry in the 1950s because of its "tranquilizing" properties. A sympatholytic, it is now used mainly for essential hypertension. Two uncontrolled studies of its use for stuttering (43, 44) reported moderately good results. In a review of tranquilizers in the treatment of stuttering, Kent (45) described four unpublished placebo-controlled studies of reserpine that had a different result. Three found no difference between the active agent and placebo. The fourth study, which involved a single subject, suggested that reserpine was more effective than placebo. Kent concluded that stutterers taking reserpine may, in fact, be more relaxed and less inhibited about speaking but that the drug has little effect on the severity of dysfluency. It is ironic that the only controlled studies of reserpine are unpublished, and it is striking that they are largely negative in outcome.

LATER STUDIES

Although the quality of drug trials in stuttering has generally improved over time, it has not always been good. Two reports from Prague (46, 47) are examples. The investigators described trials of multiple drugs, including phenothiazines, thioxanthenes, benzodiazepines, and barbiturates, given singly or in combinations to a large number of stutterers. It is impossible to determine the contribution of these agents to the improvement in speech the authors reported, since all of the patients were treated with extensive speech exercises and psychotherapy as well. The same limitations are inherent in 1968 reports from France (48) and Bulgaria (49): multiple drugs administered to stutterers receiving concurrent psychosocial treatment, without objective assessment of dysfluency rates.

Meprobamate

Meprobamate, introduced in the 1950s, was the first of the widely used "minor tranquilizers." It was

advocated for any number of "psychophysiological" and emotional disorders in which anxiety and/or physical tension appeared to play a role. It was inevitable that clinicians would try it for stuttering. Several uncontrolled studies (50–52) reported promising results. However, placebo-controlled trials with objective measures of severity of stuttering (53–55) largely failed to show the drug's superiority to placebo medication. It is no longer used for stuttering. Because less toxic and less addicting drugs are available, meprobamate is also seldom used nowadays in the treatment of anxiety disorders.

Benzodiazepines

Benzodiazepines have largely replaced meprobamate as anxiolytic and hypnotic agents. There was some early enthusiasm for using these drugs to reduce dysfluency in stuttering, but placebo-controlled studies have been negative (56–58).

Neuroleptics Other Than Haloperidol

After neuroleptics were introduced into medicine, it was inevitable that they should be tried in the treatment of stuttering. There were reports of uncontrolled studies in which chlorpromazine and trifluoperazine had some efficacy (33, 59, 60).

Goldman (61) conducted a double-blind study comparing thioridazine plus speech therapy with placebo plus speech therapy (10 patients in each group). The frequency of stuttering moments was about the same in both groups, but the thioridazine patients showed a decreased severity of stuttering, based on a 7-point scale, as judged by observers. Also, the time required to read a standardized passage (a measure of severity of stuttering) was reduced more by the drug than by the placebo. It is possible that these observed differences in drug versus placebo reflect mainly reduction in secondary symptoms in the stutterers. Few details were included in this brief report, but the results were promising.

Aron (62) conducted a double-blind, crossover study of 46 adult stutterers, comparing trifluoperazine plus amobarbital with placebo. Again, the active drugs were associated with a significant reduction in the severity but not the frequency of stuttering moments. The patients also showed a reduction in anxiety scores when they were taking the active medications, leading the author to speculate that the decreased severity of stuttering was a consequence of decreased anxiety and tension.

Haloperidol

This butyrophenone has been the subject of more treatment trials for stuttering than any other drug. Favorable results were reported in a number of uncontrolled studies (63–67) and single-blind trials (68, 69). Interest in haloperidol increased sharply after Wells and Malcolm (70) reported a placebo-controlled, dou-

ble-blind trial with objective speech measures. Thirty-six patients were randomly assigned to one of several treatment groups. Those receiving haloperidol also received orphenadrine, an antihistamine given to minimize parkinsonian symptoms. The patients receiving haloperidol, at an average dose of 4.5 mg/day, improved significantly more in the 8-week trial than those taking placebo or orphenadrine alone. The dropout rate was high. Four of the 10 patients treated with haloperidol, which included some of the best initial responders, left the project after 4 weeks. Wells (71) published a 3-year follow-up report. The patients who had completed the 8-week trial of haloperidol (but were no longer taking the medication) maintained their improvement on only one of the original three measures of stuttering severity.

In 1973 Quinn and Peachy (72, 73) published two reports on their study, which was intended as a partial replication of the Wells and Malcolm study. Their study was neither placebo-controlled nor double-blind. The results were disappointing: only four of 18 patients showed "improvement" in speech. The authors remarked that their more modest results might be related to lower dosages of haloperidol. Fifteen of their 18 subjects were unwilling to tolerate the 4.5 mg/day reported by Wells and Malcolm; the average dose was 2.5 mg/day.

Since these reports, eight additional placebo-controlled, double-blind trials of haloperidol in the treatment of stuttering have been published (74–81), all with similar and generally positive results. The following conclusions are warranted.

1. Haloperidol is more effective than placebo.
2. The drug has a greater effect on the secondary or accessory symptoms than on the primary or core symptoms of stuttering. However, these secondary symptoms are often the most distressing to the patient and the greatest impediment to effective communication.
3. Most patients must continue to take the drug to maintain improved speech.
4. Most stutterers, including those whose speech improves substantially with haloperidol, will not remain on the medication regimen because of side effects. These include dizziness, the dysphoric feeling of being "drugged," and the extrapyramidal symptoms so common with this drug. Most of the studies that provided follow-up data reported that few patients elected to continue with the drug after the initial brief trial.

These studies were conducted before the full extent of the risk of tardive dyskinesia from neuroleptics was appreciated. Given this risk, haloperidol and other neuroleptics should seldom if ever be prescribed for stuttering. Thus, we have a treatment for stuttering in adults that has some efficacy but poor patient acceptance and unacceptable risks.

The observation that haloperidol does in fact reduce the dysfluency of stutterers may have implications for the nature of the CNS dysfunction in this disorder. Although there are no well-designed studies in which the efficacy of haloperidol is directly compared with that of other neuroleptics, clinicians (like myself) who have

treated patients with these agents believe that haloperidol has specific efficacy for stuttering. Haloperidol differs from most neuroleptics in being a fairly specific blocker of dopamine receptors. Unlike chlorpromazine, for example, it has little effect on norepinephrine receptors. In addition, haloperidol has much greater selectivity for D_2 than D_1 receptors, while most other neuroleptics are nonselective dopamine receptor antagonists (82). A number of writers have suggested that stuttering may be a consequence of hyperactive, central dopaminergic systems (75, 81, 83). This may result in disturbances in neural transmission to the speech apparatus, translating into the motor breakdown we recognize as stuttering. By its potent D_2 receptor blocking effect, haloperidol might tend to normalize this hyperactive state and improve fluency.

Swift et al. (75) pointed out that haloperidol is helpful in two other disorders which share several characteristics with stuttering: motor tics and Tourette's disorder. All three disorders appear in childhood, are more common in males than females, follow a waxing and waning course, and increase in intensity with emotional stress. The sudden transient freezing often seen in parkinsonian patients, reminiscent of the sudden sustained blockages of speech in stutterers, is also related to disturbances in dopaminergic systems.

These considerations led our laboratory to test directly the dopamine hypothesis of stuttering in an experiment on the acute effects of haloperidol and apomorphine in 12 patients (84). After an initial (no drug) baseline assessment of speech, each subject received the medications under double-blind conditions in randomized order: haloperidol, 0.50 mg i.m.; apomorphine, 0.50 or 0.75 mg subcutaneously, depending on age; and normal saline, 0.50 mg i.m. Apomorphine was included in the design because it stimulates postsynaptic dopamine receptors (85) and for this reason should aggravate stuttering. Haloperidol, in a single dose, did indeed reduce dysfluency in both reading and spontaneous speech, as compared with saline placebo. Contrary to expectation, apomorphine did not increase dysfluency. Rather, there was a strong tendency for the drug to reduce stuttering in the reading task, with little effect on spontaneous speech. To account for this paradoxical outcome, we invoked the argument used by Feinberg and Carroll (86) in a somewhat similar situation. They administered apomorphine to patients with Tourette's disorder, anticipating a worsening of symptoms of that disease, but instead found some reduction. Citing recent neuropharmacologic research, they argued that low doses of apomorphine may stimulate the presynaptic, inhibitory dopamine receptors to a greater extent than the postsynaptic receptors. Thus, both haloperidol and small doses of apomorphine might lessen the symptoms of stuttering and of Tourette's disorder. This explanation might be further clarified by examining the effects of other drugs that selectively stimulate postsynaptic dopamine receptors, such as L-dopa and amphetamine.

Verapamil

In 1980 Zachariah (87) reported that a patient whom he was treating with the calcium channel blocker verapamil for a cardiac arrhythmia, and who also stuttered, showed an improvement in his speech. He then conducted a single-blind, placebo-controlled trial of verapamil in a sample of 70 adult stutterers and had striking results. Whereas none of the 20 patients who received placebo showed significant improvement, 42 of the 50 who received verapamil (40 mg b.i.d.) showed an "excellent" or "good" clinical response. Limitations of this study included the use of only the single-blind method and the absence of any objective measures of fluency. Also, the author reported no reliability checks of the judgments that patients had improved or failed to improve in their speech.

Zachariah's report stimulated two published studies that were efforts to validate his findings (88-90). Both used tighter experimental designs. Our group carried out a randomized double-blind, placebo-controlled trial using a crossover experimental design and multiple, objective measures of dysfluency (88). Ten adult stutterers served as subjects and, in randomized order, had 1-week trials of verapamil, 80 mg t.i.d., placebo three times daily, or no drug. The four measures of stuttering had high interrater reliability ($r=0.99$). The results were more modest than those reported by Zachariah. Verapamil was significantly more effective than placebo for two of the four speech measures. However, the magnitude of the improvement was small in most subjects. This may account for the fact that at 6-month follow-up, only two of the original 10 patients were still taking the medication, even though they reported virtually no side effects. However, the two subjects who elected to continue with the medication reported that the drug did indeed make a substantial difference. Both were still taking verapamil and were enthusiastic about it at a 2 1/2-year follow-up (89).

Brumfitt and Peake (90) also conducted a double-blind, placebo-controlled trial of verapamil, 80 mg b.i.d., in a crossover experimental design, with multiple measures of fluency. Fourteen subjects completed the trial. The investigators did not find evidence of improvement with the drug. It is not apparent what might account for the different outcomes of these two studies, other than the fact that we used a higher dose of verapamil (240 mg/day) than they did (160 mg/day). Also, Brumfitt and Peake did not indicate whether any of their patients elected to continue with the medication for a longer period of time.

If verapamil does reduce the severity of stuttering, the mechanism is of some interest. Zachariah (87) assumed that the drug reduces spasm of the muscles of articulation. One would expect verapamil to have a more limited effect on striated muscles (such as the voluntary muscles involved in speech production) than on smooth muscles. The latter have a smaller internal store of calcium ion and hence are apt to be more affected by verapamil's impeding the influx of the calcium ion needed

for muscle contraction. However, Brumfitt and Peake (90) called attention to a report by Walton (91) that diffuse skeletal muscle pain responded dramatically to verapamil therapy.

Some commonalities of stuttering and Tourette's disorder were mentioned in the discussion of haloperidol. It might be noted that calcium channel blockers, including verapamil, have been reported to be effective in Tourette's disorder as well (92-94). Finally, it should be noted that haloperidol, effective in Tourette's disorder and probably in stuttering, has strong calcium channel blocking activity (95).

A question that naturally occurs is whether other calcium blocking agents commonly used in hypertension and cardiac arrhythmias might be effective in stuttering. To date we have tried both nifedipine and diltiazem in individual cases (open trials) and believe that they are as effective as verapamil in selected cases.

β -Adrenergic Blockers

There are two single case reports of improvement in stuttering with β blockers. One (96) concerns propranolol, with a clear effect at a dose of 40 mg/day, and the other (97), the cardioselective β blocker betaxolol at 20 mg/day. Although these were not double-blind or placebo-controlled studies, in both reports the patients became more dysfluent again when the medication stopped. Both attributed the beneficial action to the anxiolytic properties of β blockers. However, Rustin et al. (98) conducted a well-designed double-blind, placebo-controlled study that used oxprenolol, 40 mg/day, for 31 adult stutterers and found no benefit from this β blocker.

Other Drugs

There are two reports of uncontrolled trials of the anticonvulsant carbamazepine. Goldstein (99) reported good results with two stutterers, while Rosenfeld (100) found no benefit with three patients. Neither report gives sufficient detail (measures of stuttering severity, dose of carbamazepine, etc.) to evaluate them adequately or compare them to each other.

Hays (101) reported promising results with bethanechol, an acetylcholine analogue, 20-30 mg/day. Although only two patients were studied, both had multiple drug and placebo trials in a single-blind design. Hays hypothesized that the efficacy of this cholinergic agent might be related to the fact that strongly anticholinergic drugs such as the tricyclic antidepressants may induce stuttering in susceptible persons. It should be noted that in 1949, Schaebel and Street (102) treated 10 stutterers with neostigmine, a drug owing its cholinergic action to its inhibition of cholinesterase. Their rationale was that neostigmine is useful in spastic conditions (although it has now been replaced by more effective agents). In a trial without controls of any kind, they reported decreased severity of stuttering "spasms" in their subjects.

Antidepressants are the one major category of drugs widely used in psychiatry that have not been systematically evaluated in the treatment of stuttering. Given the obsessional quality of some stuttering behavior, fluoxetine and clomipramine would be especially interesting to investigate.

CONCLUSIONS

Very diverse treatments, pharmacologic and others, have been and continue to be recommended for the treatment of stuttering. As elsewhere in medicine, this implies that no treatment has been proved to be clearly superior to the alternatives for most patients. The many pharmacologic approaches that have been used reflect different assumptions about the pathophysiology underlying this disorder. However, in some instances chance empirical observations of the effects of particular drugs on the speech of stutterers have led to hypotheses about underlying mechanisms. In any event, several of the more recent studies hold promise both for the possible therapeutic value of new classes of drugs and for possible new insights into the nature of this baffling disorder.

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Clinical Assessment of the Risk of Violence Among Psychiatric Inpatients

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***Objective:** The authors evaluated the reliability and validity of a probabilistic approach to clinical assessment of short-term risk of violence. **Method:** At admission, nurses and physicians independently rated the probability that each of 149 psychiatric patients would physically attack someone during the first week of hospitalization on a university-based locked inpatient unit. Ward behavior was measured with the Overt Aggression Scale. **Results:** There was a moderate level of agreement between nurses' and physicians' assessments of risk. Ratings of ward behavior showed an increase in the proportion of assaultive patients as the level of estimated risk of violence increased. Although the overall rate of assaults was overpredicted, there was a close correspondence between clinical estimates of patients' chances of becoming violent and the proportion of patients within each risk level who later displayed some type of inpatient aggression. **Conclusions:** The reliability and validity of short-term estimates of the risk of violence among acutely disturbed inpatients may be higher than past violence research has suggested. These findings provide preliminary support for the utility of a probabilistic approach to assessment of the risk of violence.*

(Am J Psychiatry 1991; 148:1317-1321)

Courts and legislatures continue to require that mental health professionals assess and manage their patients' dangerousness (1, 2), despite a large body of research suggesting that clinicians' ability to predict violent behavior is severely limited (3). However, previous research on predictions of violence has been limited in scope, typically involving study of long-range predictions of dangerousness of institutionalized criminally insane patients. More recent reviews of the empirical literature (4, 5) have suggested that short-term predictions among acutely ill psychiatric patients might be more accurate. Few studies have evaluated the accuracy of assessment of the risk of violence in this

context. The purpose of this study was to assess the accuracy of short-term clinical assessments of the potential for violence made at the time acutely disturbed patients were admitted to the hospital.

Although little research has been conducted on the short-term clinical assessments of the risk of violence that are made at the time of psychiatric hospital admission, the topic is important for several reasons. Patient violence is a major cause of staff injuries (6) and is most likely to occur during the first few days of hospitalization, when patients are not yet stabilized with treatment and are relatively unfamiliar to staff (7). Violence during this period is an important predictor of length of hospitalization among patients with mental disorders such as schizophrenia (8). In addition, violent behavior during the initial period of hospitalization is often considered in judicial reviews that determine whether civil commitment is warranted.

Research concerning clinical assessments of the potential for violence is complicated by the fact that clinicians have a legal and ethical obligation to intervene

Presented in part at the 98th annual convention of the American Psychological Association, Boston, Aug. 14, 1990. Received Oct. 23, 1990; revision received Feb. 28, 1991; accepted April 15, 1991. From the Department of Psychiatry, University of California, San Francisco, School of Medicine. Address reprint requests to Dr. McNiel, 401 Parnassus Ave., San Francisco, CA 94143-0984.

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when patients are assessed as dangerous. To the extent that such clinical interventions are effective, the original predictions of violence will appear to be false positives (9). Several approaches have been proposed to deal with this methodological problem. For instance, Dix (10) proposed a study in which a group of patients whom clinicians considered dangerous would be randomly selected for release, and then a follow-up would be conducted to assess how many of them actually became violent. Although such a study has not been conducted for obvious ethical reasons, there is some question about how generalizable any resulting findings would be, since in actual practice clinicians do intervene when they consider a patient at risk for violence. Another approach to this problem is to use analogue methods, such as providing clinicians with a list of test scores or case vignettes and asking them to predict whether the patients will be violent (9, 11). Although such designs enhance experimental control of variables that may affect clinical judgments, it is unclear how generalizable the results are to the clinical assessments of the potential for violence that are made in actual practice, in which the clinician is faced with a host of potentially relevant clinical and contextual variables on which to base an evaluation.

One way to advance research in this area is to conceptualize the process as assessment of the risk of violence rather than the prediction of violence (12, 13). Rather than making "predictions" of violence, clinicians, in actual practice, combine available information to make an assessment of the patients' level of *risk* of violence and then intervene in a manner appropriate to that level of risk. The accuracy of clinical assessments of the risk of violence would be supported if patients assessed as being at higher risk had a higher rate of later violence than patients assessed as being at lower risk.

One way to evaluate clinical assessments of the risk of violence is to define them as probability estimates. For example, many civil commitment laws do this explicitly when clinicians are required to justify involuntary hospitalization by determining that a patient is "more likely than not" to harm others (14, 15). In addition to this practical legal issue, there are theoretical reasons for evaluating assessments of the risk of violence as probability estimates. Early research on clinical judgments of dangerousness suggested that clinicians' judgments are limited by a number of systematic cognitive errors or "biases," such as overconfidence and ignoring base rates (3, 16). More recent developments in research on how judgments are made under conditions of uncertainty have indicated that these cognitive biases can be attenuated by framing the judgments as probability estimates (e.g., What are the chances that a person like this will become assaultive?) rather than as dichotomous yes/no decisions (e.g., Is this person dangerous?) (17, 18), particularly if the estimates pertain to a specified setting and time period for which base rate information is available (12, 13).

Although the issue of accuracy is crucial to advancing research on assessment of the risk of violence, a related

issue of fundamental importance concerns the extent of agreement among different clinicians evaluating the same patients. For example, efforts toward establishing standards of care for hospital decision making about violent patients have stressed the advantages of formulation of policy based on team input (19). At the level of decision making concerning individual patients, however, few studies have assessed the extent of agreement among clinicians. This study will provide information about this topic also.

This study addressed three main questions: 1) What is the extent of agreement between physicians' and nurses' estimates of the short-term risk of violence among acutely ill psychiatric patients? 2) What is the relationship between clinicians' estimates of the probability that patients will assault others during the first week of hospitalization and whether patients actually do assault others during that interval? and 3) What is the relationship between clinicians' estimates of patients' probability of assault and the later occurrence of milder forms of inpatient aggression, such as attacks on objects or verbal threats? We evaluated these milder forms of aggression in addition to actual assaults because such behavior frequently precedes physical assaults and therefore may be a marker for assaultive behavior (20, 21) and because such behavior typically results in interventions by staff to prevent escalation to actual assaults.

METHOD

Subjects

The study group included 149 patients admitted during an 11-month period in 1988–1989 to a university-based, locked short-term psychiatric inpatient unit. Sixty-seven (45%) of the patients were women and 82 (55%) were men. Their mean \pm SD age was 43.0 ± 19.5 years (range = 15–90 years). One hundred five (71%) were white, 24 (16%) were black, 12 (8%) were Asian, and eight (5%) were of other ethnic backgrounds. One hundred six (86%) of the 123 patients for whom both educational and occupational information was available were in the lowest two social classes according to Hollingshead's two-factor index of social position (22), i.e., classes IV and V. Thirteen (9%) of the patients were admitted voluntarily and 136 (91%) were admitted on involuntary civil commitments. Ninety-five (70%) of the involuntary patients were committed on the basis of grave disability and/or danger to self, and 41 (30%) included danger to others (often with the additional grounds of danger to self and/or grave disability) as the basis for their civil commitment.

Diagnoses were based on ICD-9-CM. Forty-two (28%) of the patients had schizophrenic disorders, 24 (16%) had manic disorders, 12 (8%) had major depressive disorders, seven (5%) had other affective psychoses, 13 (9%) had other nonorganic psychoses, 20 (13%) had organic psychotic conditions, four (3%) had

personality disorders, 14 (9%) had adjustment reactions, and 13 (9%) had other diagnoses.

Assessment of the Risk of Violence

Estimates of the potential for violence were made independently by the nurse and the physician who were involved with the admission of each patient to the ward. They used all of the information available at the time, such as clinical data from referring professionals, reports from family members, interview of the patient, and review of any available previous medical records. Each clinician estimated the probability that the patient would physically attack someone during the next 7 days on the ward by making a mark on an 11-point continuum ranging from 0% (definitely will not attack someone) to 100% (definitely will attack someone).

Twenty-two nurses and 41 physicians made ratings for the 149 patients. For each patient, only one nurse and one physician completed the rating scale. Each nurse rated a mean of 6.7 patients (range=1–18). Each physician rated a mean of 3.6 patients (range=1–21).

Overt Aggression Scale

The Overt Aggression Scale (23) is a behavioral checklist that nursing staff fill out at the end of each 8-hour shift to indicate which, if any, patients on the ward have been violent during that shift. We used the Overt Aggression Scale to increase the reliability and validity of our measurement of inpatient aggression because relying on archival sources such as incident reports often leads to underreporting of violent episodes (24). Although Overt Aggression Scale data can be translated into subscales that treat aggression as a single continuous variable, which is reported as a total aggression score, a more widely accepted strategy is to describe aggressive behavior on an ordinal scale of measurement (7, 25). Therefore, we transformed ratings on the Overt Aggression Scale subscales for physical aggression against other people, physical aggression against objects, and verbal aggression into the following three levels of violent behavior: no violence, fear-inducing behavior (verbal attacks, threats to attack people, or attacks on objects), and physical attacks on people. To enhance comparability of these findings with other research in this area (26, 27), we included only the most serious aggressive behavior exhibited by each patient in the data analysis.

RESULTS

Interrater reliability was evaluated by using an analysis of variance (ANOVA) intraclass correlation approach (28). The resulting intraclass correlation coefficient indicated a significant level of reliability of moderate magnitude ($r=0.46$, $F=2.78$, $df=148, 148$, $p<0.00001$) between physicians' and nurses' ratings of patients' chances of physically attacking someone dur-

ing the first week of hospitalization. The mean \pm SD value of the estimates of patients' probability of assault made by nurses ($31.0\%\pm 24.5\%$, range=0%–90%) was somewhat higher than the estimates made by physicians ($24.7\%\pm 21.0$, range=0%–100%).

Chi-square analyses were used to evaluate the association between clinically assessed risk at the time of admission and the occurrence of physical attacks during the first week of hospitalization. To maintain adequate expected cell frequencies for valid chi-square analyses, the patients were placed into three categories of risk according to the clinicians' estimates of their probability of assault: low (0% to 33%), moderate (34% to 66%), and high (67% to 100%). We also evaluated the relationship between estimates of the risk of violence and the occurrence of any aggression (i.e., physical attacks or fear-inducing behavior) during the next 7 days of hospitalization.

As shown in table 1, patients rated by nurses as having a higher probability of assault did engage in proportionately more assaults in the hospital. Although the proportion of patients who became assaultive increased at each level of assessed risk, the actual percentage of assaultive patients (i.e., the observed frequency) at each level was lower than would be expected based on the assessments of risk. That is, the proportion of patients predicted to be assaultive at the moderate and high levels of risk exceeded the proportion of patients who actually did become assaultive.

When the nurses' assessments of risk were compared with the later occurrence of any aggression (i.e., physical attacks or fear-inducing behavior), a significant positive association was observed (table 1). Furthermore, the actual percentage of patients who engaged in aggression within each level of assessed risk was within the range that would be expected on the basis of the probability estimates made by nurses at the time patients were admitted to the hospital. For example, 10 (68%) of the 15 patients estimated to have a 67% to 100% chance of becoming violent subsequently did engage in aggressive behavior.

As shown in table 1, a similar pattern was evident with the physicians' evaluations. Proportionately more of the patients rated by physicians as having a moderate to high probability of being assaultive than of patients rated as having a low probability of such behavior subsequently did engage in assaults in the hospital. Similarly, the physicians' ratings of risk of violence also showed a significant positive association with the later occurrence of any aggression (i.e., fear-inducing behavior or assaults) during the first week of hospitalization.

To evaluate the robustness of the findings across statistical methods, we also conducted ANOVAs to compare the mean estimated probability of assault for patients who did or did not engage in later violent behavior on the ward. The patients who became physically assaultive during the first week of hospitalization had been given significantly higher ratings of the probability of assault at admission than had patients who did not become assaultive, by nurses ($46.7\%\pm 24.7\%$

TABLE 1. Relationship Between Nurses' and Physicians' Ratings of Patients' Chances of Assault and Later Occurrence of Physical Attacks or Any Aggression During Hospitalization

Behavior in Hospital	Nurses' Ratings								Physicians' Ratings					
	All Patients (N=149)		Low ^a (N=84)		Moderate ^b (N=50)		High ^c (N=15)		Low ^a (N=111)		Moderate ^b (N=29)		High ^c (N=9)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Physical attacks ^d														
Patients who did not engage in physical attacks	123	82.6	76	90.5	38	76.0	9	60.0	97	87.4	19	65.5	7	77.8
Patients who did engage in physical attacks	26	17.4	8	9.5	12	24.0	6	40.0	14	12.6	10	34.5	2	22.2
Any aggression (physical attacks and/or fear-inducing behavior) ^e														
Patients who did not engage in any aggression	97	65.1	65	77.4	27	54.0	5	33.3	79	71.2	14	48.3	4	44.4
Patients who did engage in any aggression	52	34.9	19	22.6	23	46.0	10	66.7	32	28.8	15	51.7	5	55.6

^a0%–33% chance of physical attack.^b34%–66% chance of physical attack.^c67%–100% chance of physical attack.^dFor nurses' ratings, $\chi^2=10.5$, $df=2$, $p<0.01$; for physicians' ratings, $\chi^2=7.8$, $df=2$, $p<0.03$.^eFor nurses' ratings, $\chi^2=15.0$, $df=2$, $p<0.0002$; for physicians' ratings, $\chi^2=7.1$, $df=2$, $p<0.03$.

and 27.5%±23.2%, respectively; $F=14.46$, $df=147$, 148, $p<0.0003$) and by physicians (36.2%±20.8% and 22.2%±20.3%, respectively; $F=9.98$, $df=147$, 148, $p<0.002$). Similarly, patients who engaged in any aggression (i.e., physical assaults and/or fear-inducing behavior) during the first week of hospitalization had received significantly higher ratings of the probability of assault on admission than nonviolent patients, by nurses (42.3%±24.2% and 24.7%±22.2%, respectively; $F=19.71$, $df=147$, 148, $p<0.0002$) and by physicians (32.1%±21.7% and 20.7%±19.6%, respectively; $F=10.74$, $df=147$, 148, $p<0.002$). Overall, these results are compatible with those described in the preceding chi-square analyses and suggest that both the nurses and the physicians were able to identify patients during the admission process who were at greater or lesser risk of violence during the next week on the hospital ward.

DISCUSSION

Our results support a moderate level of reliability among clinicians in their clinical assessments of short-term risk of violence. The nurses' and physicians' assessments of the risk of violence showed a moderate correlation with each other. In addition, when the assessments of risk were categorized as high, medium, and low, nurses and physicians placed similar proportions of patients into each of these levels of risk. Apparently, the clinicians were applying similar sets of criteria in evaluating the potential for violence.

Our findings also support the validity of short-term assessments of risk made by physicians and nursing staff. Patients who were evaluated on admission as having a higher probability of physically attacking someone were overrepresented in the group of patients who later became assaultive during the first week of hospi-

talization. Although the probability estimates appeared to overpredict the rate of inpatient violence, data concerning milder forms of inpatient aggression suggest otherwise. When the predictions of physical attacks were compared with the later occurrence of any aggressive behavior, the observed frequencies were similar to what would be expected based on the probability estimates. It may be that the clinical assessments of risk identified patients who actually had a high potential for violence, but staff intervened when these patients began to escalate, thereby preventing physical attacks.

Since the same staff members who assessed the risk of violence were responsible for managing the patients' behavior, it is possible that they might have responded differently to patients depending on their perception of how dangerous the patients were. This issue was attenuated by the fact that each patient's risk assessment was made by one physician and one nurse out of a ward staff of roughly 30 nurses plus a large multidisciplinary treatment team. However, the influence of clinicians' assessments of risk on their interactions with patients is a topic worthy of further study.

The methods described in this study have promise for improving the technology of violence risk assessment. Previous efforts to study short-term violence prediction have used relatively insensitive procedures, typically nonspecific dichotomous evaluations of patients such as whether they should be civilly committed as dangerous (29–32). By permitting an examination of varying degrees of risk, the probabilistic approach to violence prediction described in this study could facilitate more sensitive assessment of the types of patients and situations in which predictions are more or less accurate. Although our study group was not large enough to address this issue, the methodology could be useful in evaluating whether assessments of the risk of violence are equally accurate for males and females (32) and for

other demographic and diagnostic subgroups. Similarly, the sensitivity of this approach to assessing the risk of violence could be useful in illuminating clinical judgment strategies that are more or less effective.

The issue of which interventions are warranted at a given level of assessed risk of violence is a matter of social policy, in which value judgments about the restrictiveness of the treatment environment, the potential damage to victims, etc., are important. Even commitment laws that authorize involuntary hospitalization based on an explicit probability estimate (e.g., "more likely than not" to harm others) are often vague about topics such as the time frame of risk and the setting in which the potential violent behavior is likely to occur. The findings of this study demonstrate the potential utility of framing assessments of risk as probability estimates that pertain to specific settings and time frames. By increasing the specificity of assessments of risk, this methodology may permit more explicit consideration of what interventions are warranted at different levels of risk of violence.

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Neuroleptic Use, Parkinsonian Symptoms, Tardive Dyskinesia, and Associated Factors in Child and Adolescent Psychiatric Patients

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Objective: The authors' goal was to determine the prevalence of and risk factors for neuroleptic-induced movement disorders in a group of psychiatrically hospitalized children and adolescents. **Method:** They evaluated the presence or absence of parkinsonism, tardive dyskinesia, and akathisia in 104 children and adolescents who were in residence in or admitted over a 6-month period to a state-operated child psychiatric center. They applied a standardized, structured assessment procedure used in research on adult and geriatric psychiatric patients and the mentally retarded. **Results:** The prevalence of parkinsonism among the 61 subjects at risk was 34% and was significantly associated with longer neuroleptic treatment periods immediately before evaluation. The prevalence of treatment-emergent tardive dyskinesia among the 41 subjects at risk was 12% and showed no association with quantitative neuroleptic treatment variables. However, patients with tardive dyskinesia were significantly more likely to have a family history of mental illness and significantly less likely to have a history of assaultive behavior. A pattern of complex pharmacological responses for parkinsonism and tardive dyskinesia, some of which are not typical of those most commonly reported in adults, was seen in this group of young patients. **Conclusions:** The study data highlight the acute sensitivity of the neuroleptic-treated child and adolescent to the development of parkinsonism, the possible role of certain patient characteristics in the vulnerability to develop tardive dyskinesia, and the possibility that neuroleptic-induced side effects experienced by children and adolescents differ in some ways from those experienced by adults. The data further strongly support the need for systematic monitoring of neuroleptic-treated child and adolescent patients for a full range of side effects.

(Am J Psychiatry 1991; 148:1322-1328)

Pediatric psychopharmacology is complicated by a lack of diagnostic specificity and important differences in drug effects between children and adolescents and adults (1-4). Pharmacotherapy in child and adolescent psychiatry, therefore, has largely been based on a "drug to symptom" approach rather than one of "drug to disease" (1, 2). Although in adult psychiatric patients the indications for the use of neuroleptics is being progressively narrowed to conditions characterized by psychotic behavior, these drugs are used for both psychotic

and nonpsychotic diagnostic categories in pediatric psychiatric patients (e.g., those with autism and conduct disorders), in hyperkinetic children, and in pediatric neurological patients (5-11).

Despite this broad use of neuroleptics in child and adolescent patients and the widespread recognition in adult psychiatry of the movement disorders associated with neuroleptic use (Parkinson's-disease-like symptoms [parkinsonism], akathisia, tardive dyskinesia, and tardive dystonia), there has been little systematic examination of the prevalence of these side effects across the broad range of child psychiatric patients. Dyskinesias have been the most studied side effect, particularly in autistic children and the mentally retarded (12-17). The examination of dyskinesias has focused primarily on withdrawal-emergent symptoms (those which occur after discontinuation of neuroleptic medication), which generally spontaneously remit in a matter of weeks or months. The prevalence of withdrawal-emergent dyskinesias has been found to be as high as 51% (13). Further, there has been relatively little effort to identify risk

Presented in part at the 140th annual meeting of the American Psychiatric Association, Chicago, May 9-14, 1987. Received Aug. 29, 1990; revision received April 17, 1991; accepted May 20, 1991. From the Nathan S. Kline Institute for Psychiatric Research. Address reprint requests to Dr. Richardson, Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY 10962.

Supported in part by Health Research Council grant HRC-13092 from the New York State Health Planning Commission.

The authors thank Frances Simpson and Ida Summers for data collection and Howard Kushner, Ph.D., for statistical consultation.

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factors that may increase a child or adolescent patient's likelihood of developing these movement disorders as a first step toward preventive intervention.

The few studies addressing neuroleptic-induced movement disorders are limited in a number of ways. First, virtually all prevalence studies of extrapyramidal side effects and tardive dyskinesia focused on either the mentally retarded or patients with autism or childhood schizophrenia. Second, only one study (18) included a systematic examination of movement disorders in a comparison group of patients from the same clinical environment who had never received neuroleptics, and this study found no difference between these two groups in the prevalence of movement disorders. Finally, the search for risk factors has tended to be limited to demographic and medication-related variables rather than clinical and family data that might suggest greater individual predisposition to these side effects.

The present study is unique in its examination of a broad spectrum of childhood psychiatric disorders, a full range of neuroleptic-induced movement disorders, specific patient-related risk factors, and the presence of nonexposed comparison patients as well as its use of standardized clinical assessments by a research team with extensive experience in rating movement disorders in adult and geriatric psychiatric patients and the mentally retarded.

METHOD

The study pool consisted of all children and adolescents who were residents at a psychiatric center at the beginning of the study or who were admitted during the following 6 months. All residents were evaluated as a clinical procedure, and consent was obtained from parents or guardians for the use of the data. Verbal assent was obtained from all of the patients before they participated in the study. A total of 133 children and adolescents were inpatients during the study period; 20 were discharged before the rating was done, three refused to be evaluated, and six did not have parental consent for inclusion in the study, leaving a study group of 104 (78% of the eligible pool).

The patients were rated for tardive dyskinesia, parkinsonism, and akathisia by using the Simpson Abbreviated Dyskinesia Scale (19), the Abnormal Involuntary Movement Scale (AIMS) (20), and the Simpson-Angus Neurological Rating Scale (21). A clinical evaluation was also performed for tardive dystonia. Subjects were evaluated by two raters (M.A.R. and G.H.), who used a 23-step movement disorder rating procedure lasting approximately 45 minutes per patient. This procedure was designed to maximize the validity of the differential diagnosis and included tested activities to increase and diminish movement counts. The reliability of the rating procedures has been previously reported (22).

The criterion measures for tardive dyskinesia were derived from the Abbreviated Dyskinesia Scale and the AIMS. The Abbreviated Dyskinesia Scale criterion for presence of tardive dyskinesia was based on a clinical

diagnosis from a consensual rating by the two raters derived from a score of mild to severe on a global scale that has been described previously (22-28). For the AIMS, the Schooler-Kane research diagnoses for tardive dyskinesia criterion (29) was used. The presence of parkinsonism was defined by a mean score of 0.4 on items 1-10 of the Simpson-Angus scale (21). The presence of akathisia was determined by a score of 2 or more on the akathisia item of the Abbreviated Dyskinesia Scale. In addition, a mannerism and stereotypy scale that had been developed for a study in the mentally retarded (22) was applied. Raters were kept blind to the patient's medication status, diagnosis, and psychiatric treatment history.

Subsequent to the rating, neuroleptic treatment histories were collected from a computerized information system at the facility and records were obtained from the patient's first treating facility and from the facility where the patient had been admitted immediately preceding the current admission. Only medication received while an inpatient was analyzed because interviews with the patients revealed a high rate of out-of-hospital noncompliance. The neuroleptic use variables that were tested for association with parkinsonism and tardive dyskinesia status were length of time since first neuroleptic treatment, chlorpromazine-equivalent dose (30) at evaluation, and continuous days of neuroleptic treatment before evaluation. Additionally, review of all of the facility records collected identified other potential risk factors, such as a family history of psychiatric hospitalization in first-degree relatives and a history of assaultive behavior in the patient.

The overall demographics of all 104 patients were studied. Side effect risk subgroups were also constructed: the 61 patients who were receiving neuroleptics at the time of evaluation were considered at risk for parkinsonism, and the 41 patients whose neuroleptic treatment histories revealed at least one period of 90 continuous days of treatment were considered at risk for tardive dyskinesia. These two risk categories were not mutually exclusive. Sixteen (26%) of the patients in the parkinsonism risk group received two side effect ratings (approximately 1 month apart), and 11 (27%) of the patients in the tardive dyskinesia risk group did so. All of the patients with tardive dyskinesia received two side effect ratings, with the exception of one adolescent who eloped from the facility after the first rating.

Group differences were tested for significance by application of the Fischer exact test and the Wilcoxon rank sum test. The problem of repeated statistical analyses was handled by using the Holm procedure (31), which is a more powerful technique than the commonly used Bonferroni method. According to the Holm procedure, the statistical test having the smallest computed *p* value is declared significant at the 0.05 level only if the computed *p* value of the test statistic is less than 0.05 divided by the number of tests. When performing multiple tests of six independent variables, therefore, a probability level of $p \leq 0.0083$ ($0.05 \div 6$) is considered significant. If one variable is thereby de-

clared significant, the probability level for significance of the next variable becomes $0.05/(N-1)$, or $p \leq 0.01 = 0.05/5$. The procedure terminates when no variable attains the required significance level.

RESULTS

Sixty-seven (64%) of the 104 patients included in the overall analyses were boys and 37 (36%) were girls. Their mean \pm SD age was 14.9 ± 2.2 years, and they had been inpatients at the facility for a mean of 95 ± 146.4 days. According to their charts, 60 (58%) had *DSM-III* diagnoses of conduct or adjustment disorders, 19 (18%) had psychoses and/or affective disorders (15 had schizophrenia, three had major affective disorder, and one had atypical psychosis), 13 (13%) had developmental disorders (primarily attention deficit disorder), and 12 (12%) had dysthymia, drug abuse, or personality disorders. The patients displayed a variety of behavioral problems; the most frequently noted were assaultive behavior (79 patients [76%]), suicidal behavior or ideation (55 patients [53%]), running away (44 patients [42%]), drug abuse (37 patients [36%]), hyperactivity (32 patients [31%]), and alcohol abuse (25 patients [24%]). A family history of psychiatric hospitalization was noted for 19 (18%) of the patients, and 37 (36%) had been physically or sexually abused. Sixty-one (59%) were receiving neuroleptics at evaluation (mean chlorpromazine-equivalent dose of 444.4 ± 514.3 mg/day) and had been receiving neuroleptics for a mean of 92.4 ± 111.0 continuous days before the rating day, and 11 (11%) were receiving antiparkinsonian agents. Among those with a history of neuroleptic treatment, the mean length of time since their first treatment was 452 ± 495.1 days. Those not receiving neuroleptics on the day of evaluation who had a previous history of receiving neuroleptics had been neuroleptic-drug-free for 189.9 ± 231.3 days.

None of the 104 patients manifested symptoms of tardive dystonia. Three patients exhibited stereotypic behaviors but did not show signs of parkinsonism, tardive dyskinesia, or akathisia.

Parkinsonism Risk Group

The parkinsonism risk group ($N=61$) showed pharmacological stability in that 46 (75%) of them had been receiving neuroleptics continuously for at least 3 weeks before evaluation. Some degree of clinical stability could also be assumed because 27 (44%) of these patients had been inpatients for at least 3 months before evaluation and only seven (12%) had been continuously hospitalized for less than 3 weeks. Twenty-one (34%) of these patients had parkinsonism. Equal numbers of these 21 patients had conduct or adjustment disorders ($N=7$ [33.3%]) and psychoses or affective disorders ($N=7$ [33.3%]). Eighteen (45%) of the 40 patients in the parkinsonism risk group who did not have parkinsonism had conduct or adjustment

disorders, and 10 (25%) had psychoses or affective disorders.

As table 1 shows, no significant differences in the median length of time since first neuroleptic treatment, the median chlorpromazine-equivalent dose at evaluation, or median age were found between patients in the parkinsonism risk group who did or did not have parkinsonism. There was a wide range in these values, however. The number of continuous days of neuroleptic treatment before evaluation was significantly higher for the patients with parkinsonism than for those without the disorder. Seventeen (81%) of the 21 patients with parkinsonism in the parkinsonism risk group exhibited assaultive behavior, compared with 31 (78%) of the 40 patients who did not have parkinsonism ($p=1.00$, Fisher's exact test, two-tailed). Although also not significantly different ($p=0.21$, Fisher's exact test, two-tailed), a larger percentage of the patients with parkinsonism (33% [$N=7$]) than without (18% [$N=7$]) did reveal positive family histories of psychiatric hospitalization in first-degree relatives.

Eleven (18%) of the 61 patients in the parkinsonism risk group were receiving antiparkinsonian drugs; three exhibited parkinsonism despite the use of these agents. Eighteen of the patients who were not receiving antiparkinsonian agents exhibited parkinsonism.

Six additional male patients, 13.3 to 16.5 years old, who were not receiving neuroleptics at evaluation also met Simpson-Angus scale criteria for parkinsonism. Thus, the study group as a whole included 27 patients who met Simpson-Angus scale criteria for parkinsonism at evaluation. The functional impairment due to parkinsonism was substantial: 17 of the 27 patients had Simpson-Angus scale total scores at least double the minimum criterion for a positive case.

Tardive Dyskinesia Risk Group

As in the parkinsonism risk group, pharmacological and clinical stability can be assumed in the tardive dyskinesia risk group. Of the 36 patients who were receiving neuroleptics at evaluation, 32 (89%) had been receiving them for at least 3 weeks. Of the 41 patients considered at risk for tardive dyskinesia, 21 (51%) had been inpatients for 3 months; only four (10%) had been hospitalized for less than 3 weeks. Five (12%) of the 41 patients had tardive dyskinesia according to our primary study criterion (the Abbreviated Dyskinesia Scale). When the quantitative Schooler-Kane research diagnoses for tardive dyskinesia criterion was used, three (7%) of the patients were diagnosed as having the disorder. All of the patients found to have tardive dyskinesia had at least one period of more than 90 days of continuous use of neuroleptic treatment in their history. The dyskinesia was treatment emergent because the tardive dyskinesia occurred while the patients were receiving neuroleptics.

Three of patients with tardive dyskinesia had conduct or adjustment disorders, and two had psychoses or affective disorders. Among the 36 patients at risk for tar-

TABLE 1. Relationship of Presence or Absence of Parkinsonism and Tardive Dyskinesia to Neuroleptic Use and Age in Psychiatrically Hospitalized Children and Adolescents Taking Neuroleptics

Variable	Condition Present			Condition Absent			Wilcoxon Rank Sum Test	
	N	Median	Range	N	Median	Range	Z	p
Parkinsonism in patients taking neuroleptics at evaluation	21			40				
Neuroleptic use								
Dose								
Milligrams per day ^a		300	50-2500		225	38-2025		
Significance							0.72	0.47
Length of current use								
Days		117	15-297		34	1-704		
Significance							2.63	0.008 ^b
Time since first use								
Days		228	15-1479		238	6-1869		
Significance							0.60	0.55
Age								
Years		15.2	10-18		15.3	9-18		
Significance							-0.60	0.55
Tardive dyskinesia in patients taking neuroleptics continuously for 3 months	5			36				
Neuroleptic use								
Dose								
Milligrams per day ^a		750	38-2500		300	50-2025		
Significance							0.45	0.65
Length of current use								
Days		141	18-168		128	11-704		
Significance							-0.02	0.98
Time since first use								
Days		319	160-525		611	135-2252		
Significance							-1.55	0.12
Age								
Years		15.5	14-17		15.4	10-18		
Significance							0.22	0.83

^aChlorpromazine equivalents.^bp=0.05 by Holm procedure.

dive dyskinesia who did not have it, however, all four diagnostic categories were represented: 17 (47%) had conduct or adjustment disorders, 10 (28%) had psychoses or affective disorders, and nine (25%) had developmental disorders or dysthymia, drug abuse, or personality disorders.

The comparisons that were tested for significance between the patients in the tardive dyskinesia risk group who did or did not have tardive dyskinesia are the same as those for the patients in the parkinsonism risk group who did or did not have parkinsonism; these are presented in table 1. The median chlorpromazine-equivalent dose at evaluation did not differ between patients with and without tardive dyskinesia, nor did the number of continuous days of neuroleptic administration before evaluation. Although the difference in total neuroleptic treatment durations between the groups with and without tardive dyskinesia was not significant, four of the five patients with tardive dyskinesia had durations well below the median for the total risk group (520 days), and the fifth was just above at 525 days. The two groups did not differ in age at evaluation.

There was a significant difference between the groups with and without tardive dyskinesia in family history of psychiatric hospitalization of a first-degree relative. Sig-

nificantly more of the patients with (80% [N=4]) than without (17% [N=6]) had such a history (p=0.003, Fisher's exact test, two-tailed; p=0.05 by the Holm procedure). Differences were also significant for a patient history of assaultive behavior. Significantly more of the patients without (89% [N=32]) than with (20% [N=1]) tardive dyskinesia had such a history (p=0.009, Fisher's exact test, two-tailed; p=0.05 by the Holm procedure). Further strengthening these findings is the fact that no associations were found in the entire study group between either a family history of psychiatric hospitalization (p=0.206, Fisher's exact test, two-tailed) or assaultive behavior (p=0.483, Fisher's exact test, two-tailed) and the neuroleptic treatment history categories of less than 3 months or 3 months or more.

The five patients with tardive dyskinesia were all adolescents; three were girls and two were boys. All five patients manifested oral-facial dyskinesia, and one also showed finger and wrist movements. Two patients had single tardive dyskinesia movements, and three (those who also met the Schooler-Kane criterion on the AIMS scale) had multiple movements and coexisting parkinsonism. Two of the latter patients were being treated with antiparkinsonian agents, which could have contributed to the greater severity of their tardive dyskinesia.

sia. There was an atypicality, however, in the medication-to-symptom relationship of these three patients in that higher neuroleptic doses were associated with more severe symptoms, in contrast to the typical finding in adults that higher neuroleptic doses are associated with less severity due to neuroleptic masking.

Atypicality in the relationship of medication to tardive dyskinesia and parkinsonism was also demonstrated by results obtained during follow-up evaluations of four of the five patients with tardive dyskinesia. One patient left the hospital before follow-up evaluation, and three of the remaining four were identified as having coexisting parkinsonism. One patient, who had two evaluations, had an atypical pharmacological response to his treatment for both tardive dyskinesia and parkinsonism. Tardive dyskinesia symptoms occurred only at the evaluation when he was receiving the lower benztropine dose, and the severity of his parkinsonism was similar at both evaluations despite a doubling of his benztropine dose. A second patient, who had three evaluations over a 3.5-month period, exhibited both typical and atypical tardive dyskinesia. Her tardive dyskinesia was typical in that the most substantial severity was seen when no neuroleptics were being administered (Abbreviated Dyskinesia Scale total score of 11 versus scores of 1 and 6) but atypical in that her second highest tardive dyskinesia score occurred when she was receiving a markedly higher neuroleptic dose than she had been receiving when she achieved her lowest score (1250 versus 300 mg/day of chlorpromazine-equivalents [molindone versus trifluoperazine]). This patient also showed an atypical parkinsonism pattern in that she had markedly more severe parkinsonism while receiving the lower neuroleptic dose (Simpson-Angus scale total score of 14 versus 7) and her parkinsonism persisted beyond neuroleptic discontinuation. A third patient, who was receiving molindone, was evaluated twice over a 5-month period and showed an atypical tardive dyskinesia pattern in that her symptoms were seen only at the evaluation done while she was receiving more neuroleptic agent and less antiparkinsonian agent. Her parkinsonism pattern, however, was typical in that she showed symptoms only while receiving half the antiparkinsonian dose and the higher neuroleptic dose. The fourth patient showed a more typical response in that higher doses of the antiparkinsonian agent resulted in fewer symptoms of parkinsonism, but never sufficiently severe to be a positive case.

Akathisia symptoms were seen in two adolescent patients (one boy and one girl). The symptoms were mild and there was no coexisting tardive dyskinesia and parkinsonism. Both of these patients had psychotic diagnoses and a history of assaultive behavior.

DISCUSSION

A major strength of this study is its focus on all patients hospitalized during a 6-month period in a chil-

dren's psychiatric center that serves as the tertiary care facility for a seven-county catchment area having few other inpatient child psychiatric resources. The study group is thus typical of a broad range of hospitalized children and adolescents and permits generalization of the findings beyond the more narrowly defined groups of subjects in previous studies, e.g., the mentally retarded (15–17) and children with autism and childhood schizophrenia (13, 14). Of interest is the high prevalence of neuroleptic use despite the relative rarity of conditions considered specific for such drugs in adult patients: psychoses and major affective disorders represented only 28% of the diagnoses among the child and adolescent patients who were receiving neuroleptics at evaluation.

This study's focus on parkinsonism contributes to the literature the first body of data on this disorder in child and adolescent patients to our knowledge. The significant association between the presence of parkinsonism and the length of neuroleptic treatment can serve as a benchmark for the clinician. The overall study findings regarding parkinsonism, however, demonstrate no easy solutions but, rather, a serious, complex, and troublesome phenomenon that demands monitoring by the clinician and more attention from the research community. The seriousness is attested to by the high prevalence found (34%), which exceeds that found in several other study groups—for instance, 24% in adults 25 to 34 years old (32, 33), 3% in developmentally disabled children (18), and 23% in children with autism and childhood schizophrenia (34)—and is comparable to a rate of 36% reported for psychotic adolescent inpatients (35).

The pharmacology of the parkinsonism was complex in that 1) symptoms were seen to remain constant despite a doubling of the benztropine dose, 2) symptoms worsened at a lower neuroleptic dose, and 3) the symptoms of 22% of the patients with parkinsonism persisted beyond neuroleptic discontinuation. Although not the focus of enough attention, this latter phenomenon has been reported in adult and geriatric psychiatric patients and neurology patients whose parkinsonism symptoms persisted up to 18 months beyond neuroleptic discontinuation (32, 33, 36–38).

The parkinsonism findings are also troublesome because we learned during the course of the study that 1) staff clinicians indicated little expectation that parkinsonism would develop, which would contribute to the underrecognition suggested by the infrequent prescription of antiparkinsonian agents, 2) in some patients the severity of their parkinsonism interfered with age-specific neuromuscular activities, such as running and swimming, and 3) the patients were well aware of these symptoms in themselves and their peers, describing them as “zombie-like” and implicating them as a reason for outpatient treatment non-compliance.

Unlike parkinsonism, the prevalence of treatment-emergent tardive dyskinesia (12%) was lower than in adult patients. This prevalence is not likely to be an un-

derestimate because of the lower probability of neuroleptic masking in children than in adults. Although the prevalence is lower than would be expected among adults, it is higher than that reported for more severely ill children or adolescents—for instance, 4% in children with childhood schizophrenia (34), 6% in autistic children (13), and 7% in mentally retarded children (17). This suggests a possible clinical risk factor for less severely ill patients.

We found no positive relationship between tardive dyskinesia and either lifetime measures of neuroleptic treatment or neuroleptic status at evaluation. Other studies examining neuroleptic use risk factors have focused primarily on withdrawal-emergent symptoms and are therefore not comparable but did show positive associations with indexes of neuroleptic use (15, 17, 34, 39). The most recent of these (13) included a few children with treatment-emergent tardive dyskinesia but reported no association between dyskinesia and neuroleptic use. What seemed to be of primary importance for the development of tardive dyskinesia in the present study were markers of patient vulnerability or lack of vulnerability.

The strong statistical association between tardive dyskinesia and assaultive behavior in the face of the small number of patients with tardive dyskinesia and the lack of a similar association for parkinsonism is intriguing. To our knowledge, this has not been reported in other work. It is all the more striking because the prevalence of that behavioral characteristic was markedly lower in the group without tardive dyskinesia than in the other three groups (patients with tardive dyskinesia and those with and without parkinsonism). This finding suggests a possible biologically mediated lack of vulnerability to tardive dyskinesia coexisting with assaultive behavior.

The significant association between the presence of tardive dyskinesia and a family history of psychiatric hospitalization and the substantially (but not significantly) higher rate of a positive family history in the group with parkinsonism than in the group without parkinsonism suggest a predisposition to these disorders occurring along with a familial loading for mental illness. Findings such as these have also been reported in adult schizophrenic patients: a family history of depression was associated with severity of parkinsonism (40) and a family history of affective illness was associated with tardive dyskinesia (24, 41). It would seem that a knowledge of family psychiatric history can be of utility as a marker in predicting a vulnerability to neuroleptic side effects.

The pharmacological pattern of the tardive dyskinesia symptoms in our study might be interpreted as either an atypicality from adult patterns or an example of pharmacological heterogeneity (42, 43), inpatient variability (44), or initial dyskinesias (45). A previous finding that the only two children with treatment-emergent dyskinesias showed a reduction in symptoms with neuroleptic reduction (46), plus the present finding from our multiple evaluations of four patients that

three of them had atypical pharmacological tardive dyskinesia patterns, suggests that atypicality is more prevalent in children and adolescents than adults. This suggestion, along with the high rates of withdrawal-emergent symptoms seen primarily in children and adolescents, raises the possibility of differing neurochemical substrates in the dyskinesias in children and adolescents compared with those in adults.

Akathisia has already been reported in child psychiatric patients (46) and in nonpsychotic children treated for Tourette's disorder (47). It has been associated with the worsening of psychosis in adults and the worsening of Tourette's symptoms in children (48, 49). Both of the patients in the present study with akathisia carried a psychotic diagnosis and were therefore at risk for a psychotic worsening or a misinterpretation of akathisia as a psychotic worsening. Either of these conditions could precipitate an increase in neuroleptic dose, which in turn could produce an even further increase in symptoms.

From a clinical perspective, this point prevalence study of neurological side effects of neuroleptics in child and adolescent psychiatric patients demonstrates that these patients are vulnerable to the development of symptoms of tardive dyskinesia, akathisia, and, particularly, parkinsonism. In addition, symptom patterns often go beyond the typical or expected. In attempting to counteract these side effects, the clinician must be aware of the complex response pattern of these disorders to pharmacological interventions. Child and adolescent psychiatric patients who are exposed to even short neuroleptic treatment durations need baseline, continual, and systematic (i.e., using rating scales) monitoring for a full range of neurological side effects. Further, side effects other than the neurological may be heightened in children or in nonpsychotic patients, as seen in children with Tourette's disorder who, although treated with low neuroleptic doses, demonstrated dose-related depression, dysphoria, hostility, aggression, fog states, and frank seizures (47).

To the research community, the presence of a clinical risk factor for treatment-emergent dyskinesia, a possible behavioral marker of reduced vulnerability to tardive dyskinesia, the high frequency of atypical dyskinesia, the high prevalence of parkinsonism, the persistence of parkinsonism beyond neuroleptic discontinuation, and the complex pharmacological pattern of parkinsonism suggest areas for future investigation in an attempt to identify the neurochemical correlates and mechanisms of these disorders. The similarities and differences between the children and adolescents of the present study and the adults reported in the literature can be heuristic for the field of movement disorders research in general. Further, findings across study groups where some neurochemical substrate differences among the groups may be known, such as age differences in monoamine oxidase levels among children, adolescents, adults, and the elderly, can be useful in generating hypotheses not possible in research approaches based on any one of these groups.

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High Nocturnal Body Temperature in Premenstrual Syndrome and Late Luteal Phase Dysphoric Disorder

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Objective: Because women with late luteal phase dysphoric disorder (LLPDD) experience symptomatic affective states predictably, they can be studied to determine whether there are biological findings related solely to the clinically symptomatic state. The authors sought to answer the question, Does body temperature change with affective state? **Method:** The core body temperature and motor activity patterns of 10 women with premenstrual syndrome (PMS), six of whom also met criteria for LLPDD, and no other psychological or medical illness were compared to those of six women with chronic, noncyclic dysphoria and six asymptomatic comparison women at four phases of the menstrual cycle. **Results:** The nocturnal temperatures of the women with PMS/LLPDD were significantly higher than those of the comparison subjects across the entire menstrual cycle, but there were no differences in nocturnal activity levels. The women with noncyclic dysphoria had a mean nocturnal temperature in the follicular phase as high as that of the women with PMS/LLPDD. The temperatures of all women were higher in the luteal phase than in the follicular phase. **Conclusions:** These findings suggest that in the future investigators should document menstrual cycle phase in all female subjects and, when studying body temperature, should carefully monitor symptomatic state in comparison subjects.

(Am J Psychiatry 1991; 148:1329-1335)

Premenstrual syndrome (PMS) is a diagnosis given to women who premenstrually experience emotional symptoms, physical symptoms, or a combination of both that do not necessarily impair their functioning. The *DSM-III-R* diagnosis of late luteal phase dysphoric disorder (LLPDD) describes a subgroup of women with PMS who experience primarily affective symptoms (depression, anxiety, irritability, affective lability). Unlike PMS, LLPDD entails severe disruption of the woman's otherwise normal psychosocial functioning in the week preceding menses. Multiple physical symptoms (breast tenderness, headaches, "bloating," weight gain) may occur, but women with physical symptoms only are excluded. A provisional diagnosis based on history must be confirmed by at least 2 months of daily symptom ratings.

Women with LLPDD provide an opportunity to study symptomatic affective states that occur predict-

ably. One can then ask whether there are biological findings related solely to the clinically symptomatic state and whether these biological findings occur in other disorders with common clinical symptoms. For example, higher than normal nocturnal core temperature has been found consistently in patients with major depression (1-10). Because depressed patients frequently report disrupted sleep, the higher temperatures have been attributed to this cause (8, 11). However, one study of unipolar depressed subjects studied in a time-isolation laboratory (7) found that their core temperatures were higher (mean difference, 0.16 °C) than those of age- and sex-matched comparison subjects across the entire day.

In this paper we report core body temperature and affective state at four phases of the menstrual cycle in 22 women. Wrist activity was used as a measure of sleep disruption.

METHOD

Subjects

Women were recruited through a newspaper advertisement for subjects for a menstrual cycle study. The

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Supported by grant MH-42194 from NIMH.

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TABLE 1. Demographic Data on Women With Late Luteal Phase Dysphoric Disorder (LLPDD), Premenstrual Syndrome (PMS), or Dysphoria and of Normal Comparison Women

Subject	Age (years)	Marital Status	Pregnancies	Births	Race	Education	Family History	Month Studied
LLPDD								
1 ^a	35	Married	1	0	White	College	Negative	November
2	40	Divorced	2	2	White	High school	Negative	October
3 ^a	35	Married	0	0	White	College	Negative	December
4 ^a	38	Married	4	2	White	College	Negative	May
5	40	Separated	2	2	White	College	Positive ^b	July
6 ^a	35	Married	3	2	White	High school	Negative	January
PMS								
7 ^a	34	Married	2	0	White	College	Negative	March
8	32	Married	2	1	Black	Graduate school	Negative	July
9 ^a	41	Married	3	3	White	College	Negative	March
10	41	Divorced	0	0	White	Graduate school	Negative	April
Comparison subjects								
11 ^{a,c}	34	Single	2	0	White	College	Negative	January
12 ^a	23	Single	0	0	White	College	Negative	January
13 ^a	30	Single	0	0	White	College	Negative	January
14 ^a	35	Single	1	0	White	High school	Negative	February
15 ^a	33	Married	1	0	White	College	Positive ^b	February
16 ^a	34	Married	3	3	White	College	Negative	September
No PMS, mild depression all month								
17	32	Married	4	3	White	High school	Positive ^{b,d}	February
18	32	Married	2	1	White	College	Negative	January
19	35	Single	0	0	White	College	Negative	March
20 ^e	27	Single	1	0	White	College	Negative	April
21	44	Divorced	2	0	White	College	Positive ^d	April
22	43	Married	2	1	White	8th grade	Positive ^{b,d}	December

^aData available for entire month of ambulatory monitoring.^bMajor depression in a first-degree relative.^cSADS-L diagnosis of minor depression in the past.^dAlcoholism in a first-degree relative.^eSADS-L diagnosis of panic disorder in the past.

women entered a 3-month prospective diagnostic evaluation if they were between the ages of 18 and 45 years, had not been pregnant or taken oral contraceptives within the previous 6 months, had had regular menses (26–32-day cycles) for the three previous cycles, had taken no medication regularly or would discontinue medication for the 4 weeks before the study, would take no medication during the period of the study, and had no chronic medical disorders.

After the women gave written informed consent, medical, sleep, and menstrual cycle histories were obtained by a physician, who carried out a physical examination, urinalysis, complete blood count, and blood chemistry screen. Results of a gynecological examination done within the past 6 months were reviewed. The Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (12) was completed, and the Research Diagnostic Criteria (13) were used to arrive at a psychiatric diagnosis, if any. Seventy-four women began the evaluation. Eleven dropped out because of pregnancy (N=1), major life crisis (N=4), or desire for immediate treatment (N=6). Retrospective histories of the 63 remaining subjects were reviewed to determine, provisionally, whether they should be diagnosed as having LLPDD, PMS, or

neither. A woman received a provisional diagnosis of PMS or LLPDD (PMS/LLPDD) if she had 1) complaints of symptoms during the last week of the luteal phase for at least the past year, 2) at least five of the symptoms specified for LLPDD in *DSM-III-R*, one of which was an affective symptom, during each symptomatic late luteal phase, 3) no evidence that the symptoms were an exacerbation of the symptoms of another disorder, and 4) symptoms that resulted in a subjective serious disturbance of her life.

All subjects then completed 3 months of daily symptom ratings. The well-known rating scale of Endicott et al. (14) consists of 21 symptoms, including both emotional and physical symptoms, each rated on a 6-point severity scale (1=absent, 6=extreme). Prospective confirmation of PMS required five or more symptoms, at least one of which was affective, to be absent or minimal for most of the early follicular phase and to demonstrate change in severity of at least 30% (2 scale points on the 6-point scale) between days 5–10 and the last 6 days of the menstrual cycle (15). The diagnosis of LLPDD was made if three additional criteria were met. The "absolute severity criterion" required a symptom to be rated absent or minimal for at least 4 days during cycle days 5–10 and to be rated

severe or extreme for one or more of the 6 premenstrual days. The "percent change criterion" required that the average symptom severity for the 6 premenstrual days exceed the average symptom severity for the 6 follicular days by 75% or more. The "effect size criterion" required that the difference between the average symptom severity for the 6 premenstrual days and the 6 follicular days exceed the standard deviation of all daily ratings for that symptom throughout the entire cycle. These criteria were applied to the 10 symptoms of LLPDD listed in *DSM-III-R*. Two out of three months that met these symptom criteria were required to confirm a diagnosis.

Forty-one women did not participate in the ambulatory monitor study for the following reasons: six were excluded for medical reasons (anemia, irregular menstrual cycles), 12 were excluded because of current psychiatric diagnoses, 13 were excluded for episodes of mental illness within the last year, three dropped out because of life changes (pregnancy, marriage, surgery), six discontinued ambulatory monitoring for various reasons (hemorrhoids, interference with work), and one woman completed a separate laboratory study but then had to return to school out of state. Twenty-two women completed 1 month of ambulatory monitoring. Of these, 10 met the prospective criteria for PMS and six of these also met the criteria for LLPDD. Six normal comparison women gave no history of premenstrual symptoms and showed no symptom changes on the prospective daily ratings. Six women given provisional diagnoses of PMS instead showed stable mild symptoms of dysphoria across all cycles for which they rated symptoms. This latter group did not meet our criteria for PMS or LLPDD or for a depressive or other mental disorder according to the SADS-L. Characteristics of the final group of subjects are shown in table 1.

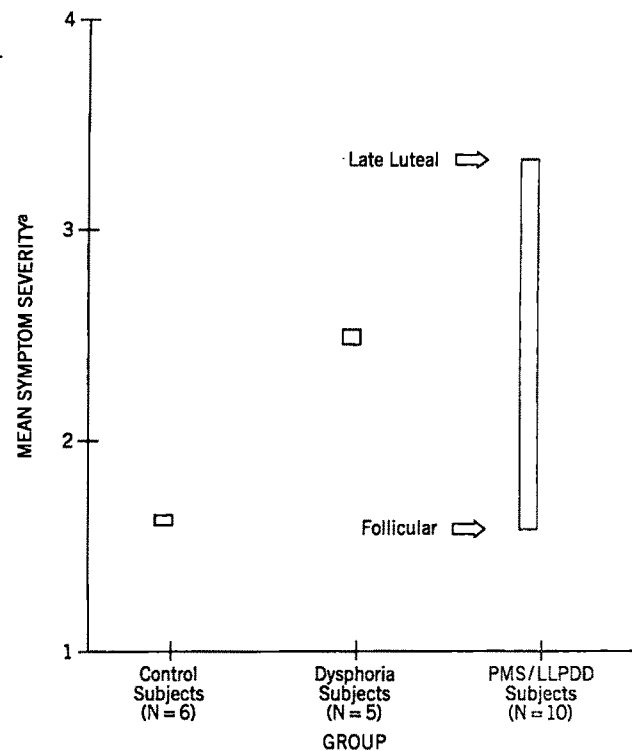
Procedure

Data were collected with an ambulatory temperature and activity monitor for four 3-day sessions within one complete menstrual cycle: early follicular phase (days 3–8), late follicular phase (0–3 days before the luteinizing hormone [LH] surge), midluteal phase (7–10 days before menses), and late luteal phase (1–3 days before menses). The first day of menses was considered day 1. Ovulation was determined by urine LH kits. All subjects had ovulatory cycles during the month of monitoring. Rectal temperature and non-dominant wrist activity were recorded at 1-minute intervals. The subjects continued to rate symptoms daily and to record bedtimes and sleep times in a sleep log.

The mean severities of the 10 LLPDD symptoms during cycle days 5–10 and the last 6 days before menses during the ambulatory monitor month were calculated for the PMS/LLPDD subjects, the comparison subjects, and all but one of the dysphoria subjects, who lost her daily symptom rating form.

Mean nocturnal (in-bed) temperature, absolute min-

FIGURE 1. Change in Severity of Combined *DSM-III-R* Symptoms of Late Luteal Phase Dysphoric Disorder (LLPDD) Between the Follicular and Late Luteal Phases in Women With Premenstrual Syndrome (PMS) or LLPDD, Women With Dysphoria, and Normal Women



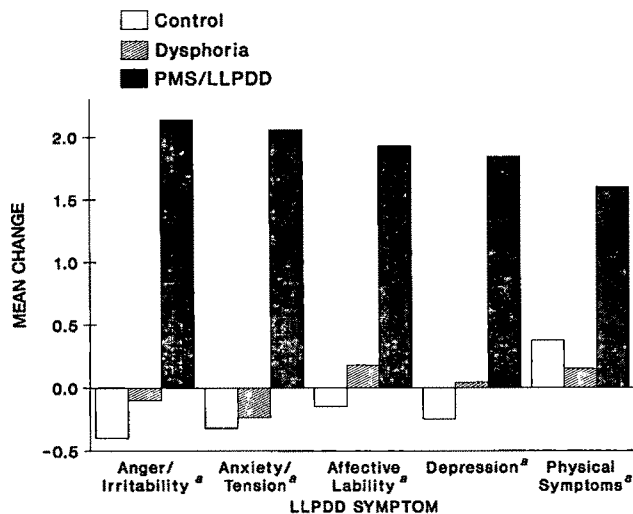
^a1=none, 2=minimal, 3=mild, 4=moderate. For each group, the bar indicates increase of symptom severity from follicular phase (lower edge) to late luteal phase (upper edge).

imum nocturnal temperature, and maximum daytime temperature were obtained from the raw data. Two independent raters determined the in-bed periods from the sleep log and wrist activity counts. The raw temperature data were replaced by values calculated with linear interpolation at 1-minute intervals. The interpolated data were then smoothed with a least-squares, low-pass filter (16) to remove high-frequency variations. The smoothed data showed a single daily minimum occurring at night and a single daily maximum occurring in the daytime. Levels and phases (clock times) of the minima, maxima, and amplitudes (maximum minus minimum) were determined from the smoothed data. Group means were calculated after the data from each subject's four sessions had been averaged.

Complete data were obtained from 12 subjects. For the remaining 10 subjects, one (N=8) or two (N=2) weekly sessions were technically flawed (probe breakage or computer data loss) or mistimed for menstrual phase.

Temperature analyses were performed by two of us (D.R.W., M.L.M.), who were blind to diagnosis. The 12 subjects with complete data sets included six sub-

FIGURE 2. Change in Severity of Specific *DSM-III-R* Symptoms of Late Luteal Phase Dysphoric Disorder (LLPDD) Between the Follicular and Late Luteal Phases in Women With Premenstrual Syndrome (PMS) or LLPDD (N=10), Women With Dysphoria (N=5), and Normal Women (N=6)



^aSignificant difference between PMS/LLPDD group and each of the other groups (t test, $p < 0.05$).

jects with PMS/LLPDD (see table 1) and the six normal comparison subjects. Of the remaining 10 subjects, four had PMS/LLPDD and six had dysphoria. Data from the early follicular session were available from each of the latter four PMS/LLPDD subjects and five of the six dysphoria subjects. Data from the late follicular session were available from three of these PMS/LLPDD subjects and five dysphoria subjects.

To determine wrist activity, the portion of each day's activity data that corresponded to the in-bed period was used to calculate an average hourly nocturnal activity count.

A two-factor repeated measures analysis of variance, with PMS/LLPDD versus comparison subject as a between-groups factor and phase of menstrual cycle as a within-subject factor, was applied to test for differences in the temperature and activity data.

RESULTS

Symptoms and Menstrual Cycle

All subjects remained true to their original prospective diagnoses during the month of ambulatory monitoring. Symptom severity in both the comparison and dysphoria subjects showed no significant change over the menstrual cycle (figure 1). The PMS/LLPDD subjects reported significantly greater changes in symptom severity during the premenstrual phase than did the normal comparison subjects (t test, $p < 0.05$) for most symptoms (affective lability, anger, anxiety, depressed mood, lack of energy, change in appetite, and physical

FIGURE 3. 24-Hour Mean Temperature Curves at Four Menstrual Cycle Phases in Women With Premenstrual Syndrome or Late Luteal Phase Dysphoric Disorder (PMS/LLPDD) and Normal Women

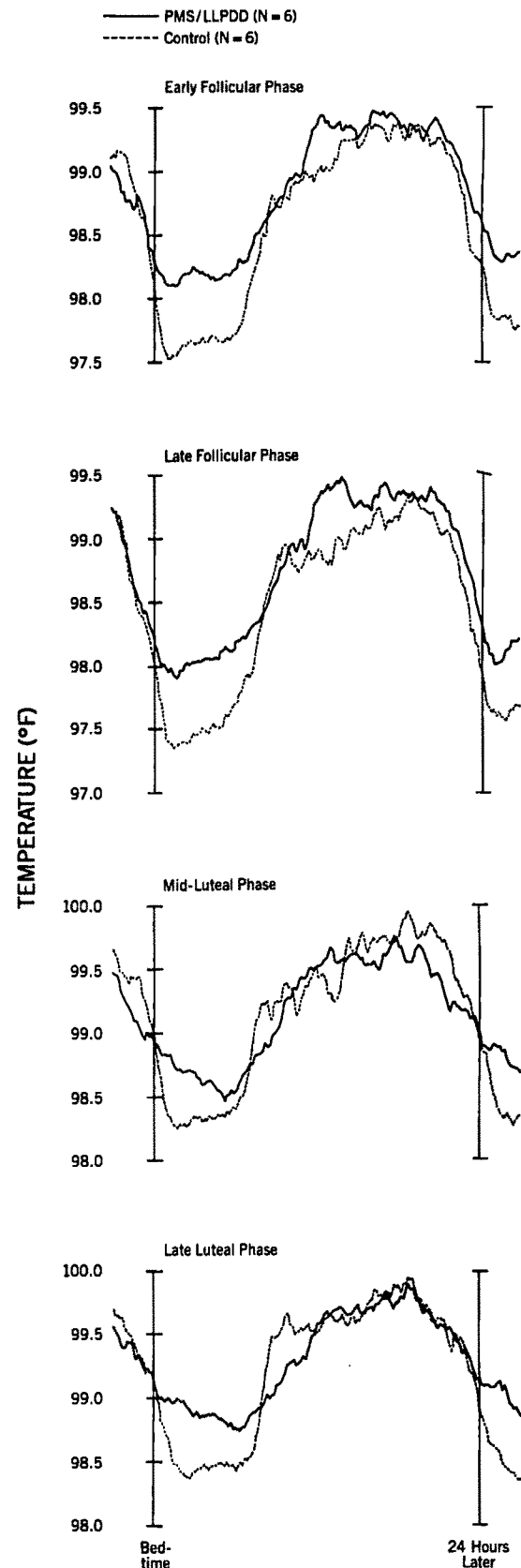


TABLE 2. Temperature Across the Menstrual Cycle of Six Women With Premenstrual Syndrome or Late Luteal Phase Dysphoric Disorder (PMS/LLPDD) and Six Normal Comparison Women

Menstrual Phase	Temperature (°F)											
	Mean of In-Bed Recordings ^a				Nocturnal Minimum ^b				Daytime Maximum ^c			
	PMS/LLPDD Women		Comparison Women		PMS/LLPDD Women		Comparison Women		PMS/LLPDD Women		Comparison Women	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Early follicular	98.2	0.2	97.6	0.3	97.9	0.2	97.4	0.4	99.6	0.2	99.6	0.2
Late follicular	98.1	0.2	97.6	0.3	97.7	0.2	97.2	0.3	99.5	0.3	99.2	0.4
Midluteal	98.6	0.2	98.4	0.4	98.4	0.2	98.2	0.4	99.8	0.3	99.9	0.3
Late luteal	98.8	0.3	98.3	0.3	98.5	0.2	98.2	0.4	99.8	0.5	99.8	0.2

^aSignificant difference between groups across entire menstrual cycle ($F=12.36$, $df=1, 10$, $p<0.01$).

^bSignificant difference between groups across entire menstrual cycle ($F=8.19$, $df=1, 10$, $p<0.02$). For all women, significantly higher minima in luteal phase than follicular phase ($F=113.25$, $df=1, 10$, $p<0.001$).

^cFor all women, significantly higher maxima in luteal phase than follicular phase ($F=19.79$, $df=1, 10$, $p<0.001$).

^dFor all women, significantly smaller amplitudes (maximum minus minimum) in luteal phase than follicular phase ($F=20.10$, $df=1, 10$, $p<0.001$).

TABLE 3. Nocturnal Wrist Activity Across the Menstrual Cycle of Six Women With Premenstrual Syndrome or Late Luteal Phase Dysphoric Disorder (PMS/LLPDD) and Six Normal Comparison Women

Menstrual Phase	Wrist Activity Counts/Hour During In-Bed Period			
	PMS/LLPDD Women		Comparison Women	
	Mean	SD	Mean	SD
Early follicular	19.6	5.0	17.3	2.8
Late follicular	16.3	8.9	22.6	15.4
Midluteal	17.0	4.3	15.6	4.2
Late luteal	22.1	5.1	22.3	4.4

symptoms). The mean changes in symptom severity were 1.5 to 2.0 scale points (25% to 33% of scale length) for eight of the 10 LLPDD symptoms. The mean changes in the four affective symptoms and the physical symptoms for the three groups are shown in figure 2.

The mean cycle lengths of the three subject groups were in the normal range and did not differ significantly.

Temperature

Temperature findings from the subjects with complete data sets are shown in figure 3 and table 2. The six PMS/LLPDD subjects had higher mean in-bed temperatures than the six normal subjects across the entire menstrual cycle. The greatest difference (0.6 °F) occurred in the early follicular phase and was nearly matched in both the late follicular and late luteal phases (0.5 °F). The nocturnal minimum temperatures were also higher in the PMS/LLPDD subjects across the cycle, whereas the daytime maximum temperatures and temperature amplitudes showed no between-group differences.

There were significantly higher minimum and maximum temperatures in all women in the luteal phase than in the follicular phase. Additionally, temperature amplitudes were significantly smaller in all women during the luteal phase. There were no significant differences between groups in the times at which the temperature minima occurred or in any Group by Menstrual Cycle Phase interactions. The mean in-bed temperature of the four PMS/LLPDD subjects with incomplete data sets was not quite as high as that of the other six PMS/LLPDD subjects during the early follicular phase (97.9 ± 0.4 °F versus 98.2 ± 0.2 °F), but it was the same (98.1 ± 0.7 °F) as that of three out of the four PMS/LLPDD subjects from whom data were available during the late follicular session.

The five dysphoria subjects with data from the follicular phase showed mean nocturnal temperatures of 98.0 ± 0.21 °F during the early follicular phase and 97.9 ± 0.2 °F during the late follicular phase. The mean nocturnal temperatures in this group were significantly higher than those of the normal group at both the early follicular ($F=3.73$, $df=1, 9$, $p<0.05$) and late follicular ($F=3.40$, $df=1, 9$, $p<0.05$) phases.

Post hoc inspection showed that in the late follicular phase, all six normal comparison subjects had a mean temperature below 97.7 °F on at least one of the three recorded nights, whereas only one of the 10 PMS/LLPDD subjects had a mean temperature below this value.

Wrist Activity

There were no significant differences in activity data between groups or menstrual cycle phases (table 3). Furthermore, when the data were pooled from all subjects regardless of diagnosis, Spearman rank order and Pearson correlations showed no consistent relationship between mean hourly nocturnal activity and mean temperature.

DISCUSSION

Potential explanations for the higher nocturnal temperatures of the women with PMS/LLPDD in our study include disturbed sleep, the thermoregulatory effects of estrogen, and altered thermoregulatory mechanisms. In major depression, as stated earlier, the finding may simply be due to disturbed sleep. However, our activity data do not support this mechanism in our subjects, and Parry et al. (17), who found somewhat higher temperature minima in women with premenstrual depression than in normal subjects, did not find more disturbed sleep when recorded polygraphically.

The known thermoregulatory effects of estrogen and progesterone may provide a partial explanation of our findings. It has long been known that progesterone raises basal body temperature, whereas estrogen lowers it (18–20) and does not block the effects of progesterone. More recently, progesterone was shown to reduce the amplitude of the circadian temperature rhythm (21, 22), a finding supported by our data, since the amplitudes were smaller during the luteal phase, when progesterone levels were higher, than during the follicular phase. Progesterone also raises the set point for all thermoregulatory responses by about 0.6 °C in human females (23, 24). In ovariectomized rats, estrogen increased self-administration of heat, suggesting that it lowers the thermoregulatory set point (20). Watts et al. (25) showed that women with “premenstrual tension” had lower estrogen values than comparison subjects throughout the follicular phase. Perhaps both our PMS/LLPDD and dysphoria subjects showed higher temperatures in part because of a relative estrogen deficiency. However, no other study has reported low estrogen levels in the follicular phase in women with PMS, nor would an estrogen deficiency hypothesis explain why the temperature difference is present only at night.

A partial failure of thermoregulation, most easily detected during sleep but unrelated to sleep disturbance per se, is a possible mechanism for the selective nocturnal higher than normal temperature in our subjects and in most subjects in studies of major depression. Fraser et al. (26) recently showed that two factors, sleep and the circadian temperature rhythm, each contribute about one-half of the 0.6 to 1.0 °F decrease in core temperature that occurs in the initial phases of sleep. The system is then thought to regulate about a lower set point (27), possibly because of the lower metabolic demand of the sleep state (28) or, more specifically, reduction in muscle activity during sleep (29). A separate in-laboratory study of PMS we are conducting suggests that the higher than normal nocturnal temperature is related to sleep and not to circadian rhythm, since the nocturnal temperature fall is blunted when our PMS subjects sleep in the laboratory, but the endogenous component appears normal during a constant routine procedure where subjects remain awake in bed for 40 hours.

In 1928 Richter (30) showed that depressed patients

have lower skin conductance and sweating than normal subjects, a finding since confirmed by others (31, 32). If this is a general feature of affective illness, a higher than normal nocturnal temperature might be due to a lack of thermoregulatory options. During the day, behavioral thermoregulatory mechanisms (seeking a cooler or warmer environment, adding or shedding clothes) are available to both normal and depressed individuals. At night, sleep, by diminishing the use of behavioral thermoregulation, may expose a functional autonomic defect in nonbehavioral thermoregulation that accompanies depressed mood.

Aminergic transmitters have been implicated in the etiology of various types of affective disorders (33), and both noradrenergic and serotonergic transmitters richly innervate the anterior hypothalamus, which is the control center for thermoregulation (34, 35). In PMS/LLPDD, the clinical expression of aminergic abnormalities may require the interplay of gonadal hormones, which are known to be concentrated not only by the preoptic anterior hypothalamus, where estrogen mediates the production of progestin receptors (36), but also by the septal and amygdala nuclei, which play fundamental roles in regulating sexual behavior, motivation, memory, and emotion (37). Progestin receptors in these latter regions are not estrogen dependent (38), but their sensitivity is modulated by noradrenergic input (37). Noradrenergic abnormalities in affective disease may therefore be expressed in LLPDD as a thermoregulatory defect throughout the menstrual cycle and as clinical symptoms only in the luteal phase, when a necessary additional factor of amygdaloseptal progesterone receptor sensitivity is active.

Our temperature findings were not specific for the diagnosis of PMS/LLPDD, however. Even the mildly dysphoric women showed higher than normal nocturnal temperatures in the early follicular phase of their cycles. Additionally, to our knowledge, core temperature has not been systematically studied in mental disorders other than major depression. An oral temperature study of institutionalized patients with chronic schizophrenia (39) showed the mean daytime temperature of the patients to be similar to that of normal subjects, but the evening and nocturnal (6:00 p.m. to 3:00 a.m.) temperatures to be *lower*. A nonschizophrenic patient group in the same study had *lower* oral temperatures than the normal group throughout the 24 hours of study. Unfortunately, this study was poorly controlled for medications (drugs discontinued for only 24 hours and in only 60% of the patient subjects), for activity levels (the comparison subjects were ambulatory, but the patients were confined to their wards), and, importantly, for male/female influences. These differences may account for the patients' lower temperatures. Nevertheless, the differences found were in the opposite direction from those we found in PMS/LLPDD and mildly dysphoric subjects, and our finding of higher than normal nocturnal temperatures is similar to findings in patients with major depression.

Further studies are needed to confirm our results

(the number of subjects in this study was small) and to test hypotheses regarding the source of the high core temperature. Our confirmation that the entire circadian temperature pattern is raised and flattened during the luteal phase in all women suggests that future investigations of menstruating women should take menstrual cycle phase into account. In addition, our finding of higher than normal nocturnal temperature in women with only mild dysphoria suggests that "normal" comparison subjects for studies of body temperature need to be very carefully defined and monitored for both menstrual cycle phase and subjective mood state.

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Cognitive Outcome Following Tricyclic and Electroconvulsive Treatment of Major Depression in the Elderly

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Objective: This study sought to ascertain the affective and cognitive outcome after tricyclic and electroconvulsive treatment of elderly medical-psychiatric patients meeting diagnostic criteria for major depression, some of whom had normal cognitive functioning and some of whom were cognitively impaired before treatment. **Method:** Patients who met criteria for major depression on the basis of a structured diagnostic interview and who scored 17 or more on the Hamilton Rating Scale for Depression were evaluated with the Mattis Dementia Rating Scale. The patients were then treated in a nonrandom manner with either tricyclic antidepressants or ECT (followed by tricyclic maintenance therapy). The majority of the patients treated with ECT had not responded previously to tricyclics. Follow-up psychometric testing was repeated in 6 months. **Results:** Among the patients with normal pretreatment cognitive functioning, cognition was generally stable. Among the patients with pretreatment cognitive impairment, a substantial number—including those receiving ECT—demonstrated improvement in cognition. While the majority of patients improved with respect to both their affective and cognitive states, certain treatment-refractory subgroups were nevertheless identified. **Conclusions:** The data suggest that cognitive dysfunction associated with depression may improve after treatment in a substantial number of elderly patients, including those receiving ECT. Relapse rates, however, may be relatively high, and residual symptoms may persist, which emphasizes the need for optimal initial and long-term antidepressant strategies for this population. (Am J Psychiatry 1991; 148:1336–1340)

Several recent reports have focused attention on the evaluation and treatment of elderly patients with depression and cognitive impairment (1–10). Although depression can usually be treated when Alzheimer's disease is clinically manifest (11–14), there have been relatively few published outcome studies of neuropsychological functioning after antidepressant therapy in geriatric patients with mixed patterns of depression and cognitive impairment when the primary etiology of the patients' cognitive dysfunction was initially unclear (8–10). In this uncontrolled naturalistic study, cognition and affect were evaluated before and after treatment in two groups of geriatric patients with major depression:

one group with normal pretreatment cognitive functioning and the other with preexisting cognitive impairment of uncertain etiology. At 6-month follow-up, the two groups were compared with respect to cognitive and affective changes after tricyclic antidepressant and electroconvulsive therapy.

METHOD

All of the subjects were 55 years of age or older and were initially inpatients on a combined medical-psychiatric unit. Most patients were referred to this program because their depression had been refractory to standard pharmacologic antidepressant regimens, and others were referred because of concurrent medical illness that complicated their treatment. The most frequent medical disorders that were an active focus of treatment during these patients' hospitalization were advanced cardiovascular disease (American Society of Anesthesiologists classes II–IV), including hypertension and congestive heart failure (54%), orthopedic disorders, advanced osteoporosis, and rheumatoid arthritis (21%), gastroin-

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Supported by NIMH grant MH-43549 and National Alzheimer's Association grant PRG-87-158.

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testinal disorders (19%), chronic lung disease (13%), and diabetes mellitus (8%).

The study was approved by the institution's human investigations committee, and all patients or their guardians signed informed-consent forms before participating. Exclusion criteria were history of stroke, cerebrovascular disease, or multi-infarct dementia (by CT scanning); recent or remote history of alcoholism or head trauma, or any other disorder suggesting a source of cognitive dysfunction other than possible early Alzheimer's disease or major depression; and use of medications well-known to induce organic depressive disorders (steroids, β -adrenergic blocking agents, α -methyldopa, reserpine).

Patients received extensive medical, neurological, and laboratory assessments to rule out treatable medical causes of their depression and cognitive dysfunction. These included SMA-18, RPR, CBC, urinalysis, thyroid function tests (T_4 , T_3 , TSH), serum B_{12} and folate levels, brain CT scanning, EEG (to rule out structural lesions and epileptiform foci), chest X-ray, and ECG.

To participate in the study, subjects had to meet the diagnostic criteria for major depression as determined by the Structured Clinical Interview for DSM-III-R—Patient Version (SCID-P) (15), administered by a research assistant. Independent clinical confirmation of the diagnosis of major depression by the attending psychiatrist and supervising neuropsychologist was required. Subjects also had to have a score of 17 or more on the 21-item Hamilton Rating Scale for Depression (16).

Psychometric assessment was performed after a minimum 7- to 10-day washout period for withdrawal of psychotropics and medications known to affect cognitive status. Patients also received neuropsychological assessment with the Mattis Dementia Rating Scale (17).

Primary treatment was then instituted in a nonrandom, uncontrolled manner with either a tricyclic antidepressant or ECT on the basis of the following clinical criteria. Initial treatment with a tricyclic was begun, in general, if a patient had *not* previously received a trial of tricyclic antidepressant treatment of at least 4 weeks' duration with adequate dosage. The choice of antidepressant was based on multiple clinical considerations, including sensitivity to side effects (depending on the patient's medical condition) and previous positive or negative response to medication. Because of the age and medical fragility of these patients, doses were, on average, relatively lower than those usually considered therapeutic for middle-aged patients. The types of antidepressants and mean \pm SD oral doses for the 25 patients treated primarily with medication only (no ECT) who completed the study were as follows: doxepin ($N=18$, 72.0%), 116.7 \pm 63.59 mg/day; desipramine ($N=3$, 12.0%), 75.0 \pm 66.14 mg/day; amoxapine ($N=1$, 4.0%), 200 mg/day; nortriptyline ($N=1$, 4.0%), 75 mg/day; maprotiline ($N=2$, 8.0%), 87.5 \pm 17.70 mg/day.

Antidepressant serum levels were ascertained when patients were judged not to be responding to treatment or when they were experiencing significant side effects.

The mean \pm SD serum level was 67.0 \pm 27.55 ng/ml in the 14 patients whose doxepin levels were obtained during the initial hospital treatment phase. The serum level was 115.2 \pm 86.72 ng/ml in the 12 patients whose doxepin levels were evaluated at 6-month follow-up.

The choice of treatment with ECT for a patient was based on one or more of the following criteria: 1) failure to respond to at least a 4-week trial of a tricyclic antidepressant at an adequate dose and serum level, 2) serious medical debilitation due to severe malnutrition or dehydration, 3) potential hazard of antidepressant treatment because of the risk of heart block, severe orthostatic hypotension, or other medical factors, 4) a clearly defined historical pattern of resistance to antidepressant medication and responsiveness to ECT.

ECT was given three times a week, with unilateral electrode placements over the nondominant hemisphere according to the D'Elia placement method and thiopental and succinylcholine for anesthesia, to induce a generalized seizure of at least 30 seconds' duration documented by EEG monitoring. The mean \pm SD number of treatments per patient was 9.6 \pm 2.8. If it was feasible from the standpoint of tolerating side effects, patients received maintenance antidepressant medication following ECT. Ninety percent ($N=27$) of the 30 ECT-treated patients who completed the study received maintenance antidepressants; three patients did not receive them because of noncompliance with the regimen or inability to tolerate side effects. The types and mean \pm SD oral doses of maintenance antidepressants were as follows: doxepin ($N=21$, 70.0%), 123.8 \pm 52.72 mg/day; desipramine ($N=1$, 3.3%), 50 mg/day; fluoxetine ($N=3$, 10.0%), 20 mg/day; and lithium carbonate ($N=2$, 6.7%), 600 mg/day. (Two patients in the follow-up period developed hypomanic episodes and were suspected to have had latent bipolar illness, even though overt manic episodes had not been identified in their psychiatric histories. These patients were eventually given lithium alone as their prophylactic agent.)

Ten patients were noted to have varying degrees of delusional symptoms. Seven of these were treated with low doses of adjunctive neuroleptics; the doses were loxapine ($N=3$), 10 mg/day; haloperidol ($N=2$), 2 mg/day; trifluoperazine ($N=1$), 2 mg/day; and thiothixene ($N=1$), 4 mg/day. In addition, six patients exhibited residual agitation requiring low doses of neuroleptics; the doses were trifluoperazine ($N=1$), 2 mg/day; loxapine ($N=3$), mean \pm SD=11.7 \pm 6.2 mg/day; and haloperidol ($N=2$), 2 mg/day.

Following discharge from the hospital (the average length of stay was 26 days), patients were seen in routine clinical follow-up on an average of every 2–3 weeks. Psychometric reassessments were performed approximately 6 months after hospital discharge. The mean \pm SD time to follow-up for such testing after hospital discharge was 30.0 \pm 11.2 weeks.

The data were analyzed after dividing the patients into two major groups: those with major depression but no evidence of cognitive impairment before treatment and those who had both major depression and cogni-

TABLE 1. Depression and Dementia Scores of 55 Elderly Patients With Major Depression, With or Without Pretreatment Cognitive Impairment, Treated With Tricyclic Antidepressants or With ECT Followed by Antidepressant Prophylaxis

Group	Score on the Hamilton Rating Scale for Depression				Score on the Mattis Dementia Rating Scale ^a			
	Pretreatment		Posttreatment		Pretreatment		Posttreatment	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Patients treated with tricyclic antidepressants only (N=25)								
Normal cognitive functioning (N=9)	26.11	3.26	12.78 ^b	7.40	135.56	5.34	134.22	6.24
Impaired cognitive functioning (N=16)	27.25	7.78	10.38 ^b	8.26	111.44	12.33	119.00 ^c	25.90
Patients treated with ECT (N=30)								
Normal cognitive functioning (N=11)	29.27	8.28	13.27 ^d	11.35	135.82	2.89	133.46	8.86
Impaired cognitive functioning (N=19)	33.95	8.17	14.68 ^d	10.84	107.42	17.85	123.37 ^e	12.77

^aLower scores indicate greater cognitive impairment. Maximum score (highest cognitive functioning)=144.

^bSignificant posttreatment improvement in depression score for both cognitive groups ($F=112.87$, $df=1, 23$, $p<0.0001$).

^c $N=15$ for posttreatment dementia scale score.

^dSignificant posttreatment improvement in depression score for both cognitive groups ($F=78.26$, $df=1, 28$, $p<0.0001$).

^eSignificant posttreatment improvement in dementia score for the group with impaired cognitive functioning ($F=9.71$, $df=1, 28$, $p<0.005$).

tive impairment before treatment. Subjects who had scores of 130 or more on the Mattis Dementia Rating Scale before treatment were considered cognitively intact, and subjects who had scores below 130 were considered cognitively impaired.

A total of 77 patients evaluated over a 3-year period initially met the eligibility criteria and were entered into the study. Nineteen (24.6%) of the patients originally evaluated were dropped from the study or completely lost to follow-up, usually because of geographical relocation to distant regions of the country or refusal to cooperate with follow-up testing. There were missing data on certain measures for three other patients, so the data for these patients were not used in the analyses of outcome. Thus, the analyses included the data for 55 subjects who completed the study.

RESULTS

The patients who were lost to follow-up (noncompleters) were compared to the patients who completed the study in terms of gender, age, education, severity of depression, and cognitive impairment. Statistical analyses revealed no significant differences between study completers and noncompleters with respect to education level ($t=-0.55$, $df=70$, $p=0.58$), percentages of men and women ($\chi^2=2.11$, $df=1$, $p=0.15$), severity of depression (Hamilton scale score) ($t=0.44$, $df=71$, $p=0.69$), or severity of cognitive impairment (Mattis scale score) ($t=-0.95$, $df=71$, $p=0.35$). Noncompleters were significantly younger than completers ($t=3.86$, $df=72$, $p<0.001$). The mean \pm SD age of the noncompleters was 66.5 \pm 7.30 years.

The group of patients who were cognitively intact prior to treatment consisted of 20 individuals (seven male and 13 female) with a mean \pm SD age of 71.2 \pm 7.07 years and 12.3 \pm 4.09 years of education. The group who were cognitively impaired before treatment consisted of 35 patients (nine male and 26 female) with a mean age of 72.5 \pm 6.96 years and an education level of

10.6 \pm 3.11 years. There was no statistically significant difference between the two groups in terms of gender, average age, or educational background.

No attempt was made to address treatment differences between the tricyclic antidepressant and ECT groups directly, since the patients were not randomly assigned to these groups. Patients in the ECT group were, for the most part, individuals for whom treatment with antidepressants had failed, and so they differed from patients in the antidepressant treatment group from the outset. Thus, analyses for each of the two major treatment modalities are reported separately.

Group Treated With Tricyclic Antidepressants

Mean Hamilton depression scores before and after treatment for the patients treated with antidepressants alone are presented in table 1. A two-factor repeated measures analysis of variance (ANOVA) showed that there was significant improvement in depression in both the cognitively intact group and the cognitively impaired group after treatment. No significant differences between the two groups in Hamilton depression scores before or after treatment were observed.

Clinical outcome was also examined by operationalizing "clinically meaningful" improvement. Patients who achieved a 50% or more reduction in their Hamilton depression scores or a score of less than 13 were classified as showing such improvement (18).

Seventeen (68.0%) of the 25 patients treated with tricyclic antidepressants demonstrated a clinically meaningful response to treatment; five of these were cognitively intact and 12 were cognitively impaired before treatment. There was no significant difference in the percentages of cognitively intact and cognitively impaired patients who exhibited clinically meaningful versus no clinically meaningful improvement ($\chi^2=0.31$, $df=1$, $p=0.58$, with continuity correction).

To examine the effects of treatment on cognition at outcome, a two-factor repeated measures ANOVA was

completed using the total score on the Mattis Dementia Rating Scale for the groups with and without cognitive impairment treated with antidepressants only both before and 6 months after treatment (table 1). No statistically significant change was observed in the dementia scale scores from before to after treatment, nor was the interaction term significant, suggesting that cognitive functioning remained stable for both cognitive groups who underwent chronic antidepressant treatment.

Group Treated With ECT

The mean Hamilton depression scale scores for the ECT treatment group before and after treatment are presented in table 1. A two-factor repeated measures ANOVA showed that there was significant improvement in depression. No significant differences in depression severity between cognitively intact and cognitively impaired patients treated with ECT were observed either before or after treatment.

Nineteen (63.3%) of the 30 ECT patients (eight cognitively intact and 11 cognitively impaired) exhibited clinically meaningful improvement as defined previously. There was no significant difference in the percentages of patients in the two cognitive groups who exhibited clinically meaningful versus no clinically meaningful change ($\chi^2=0.18$, $df=1$, $p=0.68$, with continuity correction).

Mean pretreatment and posttreatment dementia scale scores for the ECT treatment group are presented in table 1. A two-factor repeated measures ANOVA revealed a statistically significant interaction indicating that the cognitively impaired patients exhibited a significant improvement in dementia scores following ECT. No similar change was noted in the cognitively intact patients' scores from before to after treatment, possibly because of ceiling effects.

Rehospitalization Rates

The number of patients in each treatment group who required rehospitalization for depression within 1 year of initial admission and discharge was determined through a review of their medical charts (one patient from each group was lost to follow-up at 1 year). Approximately 28% ($N=8$) of the 29 ECT-treated patients were rehospitalized for depression within 1 year; 25% ($N=6$) of the 24 antidepressant-treated patients were readmitted.

DISCUSSION

The results of this study suggest that not only is cognitive functioning generally stable at 6-month follow-up after geriatric patients are treated for depression, but in some patients cognitive functioning is actually improved, as was evident in some of the patients who received ECT with maintenance antidepressants. In a considerable number of patients, almost complete nor-

malization of cognitive functioning was observed clinically, despite the fact that before treatment several of these patients had scored below the Mattis scale cutoff levels for dementia.

Several comments are pertinent regarding three subgroups of patients that were identified among the group of 35 patients who were cognitively impaired before treatment. Eight of these patients (four from the antidepressant-only group and four from the ECT group) were observed to have a complete reversal of pretreatment cognitive dysfunction, with a return to normal levels, indicating that their initial cognitive dysfunction was most likely related to the presence of major depression. Thus, in retrospect, this subgroup represented patients who have traditionally been referred to as having the classic "pseudodementia" syndrome (5, 19).

Another 15 patients who were cognitively impaired before treatment (seven from the ECT group and eight from the antidepressant-only group) achieved remission of depressive symptoms but remained cognitively impaired, suggesting the possibility of underlying early dementia. Alternatively, this persistent cognitive dysfunction could possibly be explained by anticholinergic side effects of the tricyclic antidepressant treatment.

Although as a group, patients with pretreatment cognitive impairment improved, a third subgroup of 12 patients improved minimally in cognition and in depression. For these patients, it was not entirely clear whether the lack of improvement was due to failure of their depression to respond to treatment, effects of co-existent dementia, or anticholinergic side effects of the antidepressants. In contrast, in the patients who were cognitively intact before treatment, cognition did not change after treatment with either tricyclic antidepressants only or ECT and maintenance antidepressant therapy.

The 1-year rehospitalization rate for the entire group of patients (26.4%) was relatively high and indicates the need to standardize optimal prophylactic biological and psychosocial treatment modalities, particularly since the value of maintenance antidepressant therapy is now well-established for younger adult and middle-aged patients (20, 21). Nevertheless, even for middle-aged patients, the chronicity rates for major depression may be as high as 20% after an index episode, and 15%–20% of patients who initially improve show signs of relapse within a year (20, 22–25). Moreover, relapse rates for recently hospitalized and more treatment-resistant groups may be as high as 40% (21). Relapse rates for ECT-treated patients within several years of treatment have been estimated to be between 25% and 40% (26).

There were several weaknesses in this uncontrolled, naturalistic outcome study. Tricyclic therapy was instituted in a relatively uncontrolled manner, and tricyclic serum levels were not routinely monitored. Standardization of the medication treatment protocol and more rigorous attention to monitoring antidepressant serum levels could possibly have improved the response rate and decreased the rehospitalization rate. Although

it was not possible from the standpoint of utilization review, a minimum 2-week drug washout period would have been more desirable than our 7- to 10-day minimum before neuropsychological testing.

In summary, our data suggest that cognitive dysfunction associated with depression may improve substantially in a considerable number of depressed elderly patients after treatment. Despite these positive findings, however, subgroups of patients who do not improve with treatment exist, and chronic depressive symptoms may persist. The data suggest, however, that the majority of elderly patients with major depression are likely to have stable or improved cognitive functioning after treatment, including those who receive ECT.

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Identification and Characterization of Greater Mood Variance in Depression

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Objective: The authors sought to assess the quantity and quality of mood variation in depressed persons. **Method:** Using a visual analogue scale, they compared variation of mood in a group of patients (N=9) with a DSM-III-R diagnosis of depressive disorder and in a group of nondepressed subjects (N=9) over 12 consecutive hours. To quantify mood variation for each subject, the authors computed the standard deviation of each subject's 13 mood ratings on the visual analogue scale. To characterize the quality of mood variation within each subject, they plotted each subject's mood ratings as a function of time and applied complex demodulation to confirm cyclical patterns of mood variability (ultradian cycles). **Results:** The depressed group demonstrated greater mood score variability over the course of the day. Both groups demonstrated ultradian cycles and circadian trends; however, the depressed group demonstrated ultradian cycles of significantly greater amplitude than the nondepressed group. **Conclusions:** Repeated assessments of mood at different times of the day may be necessary to obtain an accurate impression of a patient's mood state. Further, the mechanism of depressive disorders may include a deregulation of a normal oscillatory mood variation pattern.

(Am J Psychiatry 1991; 148:1341-1345)

Depression is often viewed as a persistent state of dysphoria. Mood is often considered to be a stable state over the course of the day. Although recent discussions of rapid cycling of mood over a period of days in depressed patients have appeared in the literature (1), rapid changes in mood within the course of the day have received relatively little attention.

Variability of biological systems with time is an area of increasing study in the field of medicine. Studies of cyclical variability have examined circadian rhythms (cycles of 24 hours), infradian rhythms (cycles of more than 24 hours), and ultradian rhythms (cycles of less than 24 hours) (2). Cyclical variations have been reported in temperature, blood pressure, and many other physiological variables (3). Comprehensive reviews of the basic properties of biological rhythms in medicine are available (4, 5).

Studies of cyclical variation in psychiatry have focused predominantly on circadian rhythms, such as daily variations in serum cortisol (6), thyroid-stimulating hormone (TSH) (7), and melatonin (8) levels.

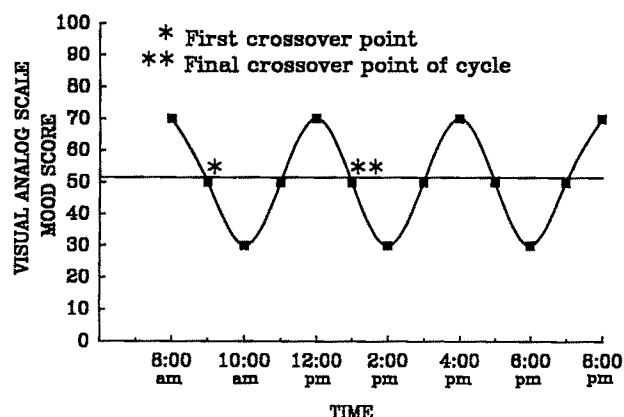
Circadian cycles of symptom intensity in depression have also been well studied. A low morning mood, followed by improvement throughout the day, has often been associated with endogenous depression. Dysphoric mood is the symptom most commonly reported to show circadian variation (9). In a review of seven studies, Tolle and Goetze (10) reported in 1987 that 10%–76% of depressed patients demonstrate circadian rhythms of mood.

The study of ultradian rhythms is a relatively new area of psychiatry. Ultradian rhythms in dominant EEG frequency (11), sleep latency (12), and cognitive performance style (13) have been reported in normal volunteers. Ultradian rhythms have also been reported in a broad range of other measures such as solitary and social behavior in monkeys (14) and hypnotic suggestibility in humans (15). An ultradian rhythm in the REM sleep of depressed patients has been recently described (16). A thorough review of the literature with the Medical Literature Analysis and Retrieval System (MEDLARS), however, revealed only a single report of ultradian rhythms of mood (17). In this paper we report, for the first time, on a study designed to identify and characterize mood variations in both depressed and nondepressed persons. We hypothesized that depressed persons demonstrate greater hour-to-hour mood variability than nondepressed persons.

Received Sept. 19, 1990; revision received March 14, 1991; accepted April 17, 1991. From Walter Reed Army Medical Center and the Henry Phipps Psychiatric Clinic, Johns Hopkins Hospital, Baltimore. Address reprint requests to Dr. Hall, Department of Psychiatry, Walter Reed Army Medical Center, Washington, DC 20307.

The authors thank Dr. Gregory Belenky for his assistance.

FIGURE 1. Crossover Point Identification for Determination of Length of Ultradian Mood Cycle



METHOD

Subjects for this study included both inpatients and nursing staff from two inpatient units of the Henry Phipps Psychiatric Clinic at the Johns Hopkins Hospital. Prospective study subjects were recruited on the basis of their continuous presence on the psychiatric inpatient units under study and their availability to give 13 consecutive hourly reports on their mood state between the hours of 8:00 a.m. and 8:00 p.m. We selected these times to ensure that subjects who retired early could receive the same number of mood assessments as those who retired later. Psychiatric residents, who were blind to both the purpose and design of the study, were asked to recruit inpatients who either carried an incontrovertible *DSM-III-R* diagnosis of depressive disorder or who unequivocally had no evidence of depression. Nonpatient participants were recruited from the same inpatient units by the investigators. Prospective subjects were excluded from consideration if they had evidence of cognitive impairment (a Mini-Mental State examination score of less than 27) (18), if they were actively hallucinating or delusional, or if they had any evidence of withdrawal from alcohol or any other psychoactive substance.

The study subjects ($N=18$) were divided into two equal groups. The depressed group consisted of inpatients with a *DSM-III-R* diagnosis of depressive disorder: six with a major depressive episode (all unipolar), two with a depressive disorder not otherwise specified, and one patient in the depressed phase of bipolar disorder (type II). The nondepressed group consisted of five volunteers from the nursing staff and four inpatients with paraphilia disorders, none whom had any evidence of depressive symptoms. The depressed group (mean age=33 years) included three men and six women, and the nondepressed group (mean age=35 years) included five men and four women.

Using the Hamilton Rating Scale for Depression (19) and the Montgomery-Asberg Depressive Rating Scale (20), we assessed the mood state of each subject on the morning of testing. Changes in mood through-

out the study day were measured using the Visual Analogue Mood Scale, a highly reliable tool for repeated measurements of mood (21). One of us (D.P.H.) administered the scale to each subject at 1-hour intervals for a 12-hour period commencing at 8:00 a.m. Subjects were instructed to place a mark along a 100-mm line at the point that best represented their present mood state. The extremes of the scale were labeled as "worst, sad" (left pole) and "best, happy" (right pole). In order to compare the level of depression of the depressed group to that of the nondepressed group, we employed two-tailed *t* tests on the differences between the mean Hamilton and Montgomery-Asberg scale scores of the respective groups. Similarly, we employed a two-tailed *t* test to compare the difference between the means of the nine sets of visual analogue scale ratings of the respective groups. To measure the variability of mood for each patient, we computed the standard deviation of each patient's 13 visual analogue scale ratings. To test the hypothesis that depressed persons experience greater mood variability than nondepressed persons, we performed a two-tailed *t* test on the logarithmic transformation of standard deviations of visual analogue scale ratings of individuals in the two groups.

With our small sample size, it is possible that the underlying assumptions required to apply parametric statistical methods to our data may not be valid; thus, we also applied nonparametric methods to the same data. We employed the Mann-Whitney test, an appropriate nonparametric technique for analyzing small samples (22). The *U* statistics and their associated probabilities are reported. In this study, all probability values derived by parametric *t* tests were verified by this nonparametric method.

In order to detect temporal trends or patterns in the variability of mood throughout the day, we plotted visual analogue scale ratings as a function of the hour of the day for each subject. A linear regression analysis was performed on each of these plots in order to measure its slope. This slope was then used to estimate the circadian trend in mood or general elevation in mood over the course of the day, since detection of a full circadian cycle was not possible because of the limited duration of testing (12 hours).

We detected the presence of ultradian rhythms in the following manner. Using the plotted data and linear regression line, we estimated any observed periodicity by measuring the distance between the first crossover point (point where cycle intersects the regression line) and the final crossover point of each full cycle, as depicted in figure 1. We then used complex demodulation to determine the amplitude of the cycle and a correlation coefficient (r^2) to describe the goodness of fit of the original data to an ultradian cycle model (23). Finally, we compared the characteristics of the ultradian cycles of the depressed group to those of the nondepressed group by employing two-tailed *t* tests on the differences between the mean amplitudes and mean periods of the two groups.

TABLE 1. Depression Inventory Scores and Corresponding Mood Variation Data for Inpatients With a *DSM-III-R* Depressive Disorder and Nondepressed Comparison Subjects

Group and Subject	Hamilton Depression Scale Score ^a	Montgomery- Asberg Depression Scale Score ^b	Visual Analogue Mood Scale Score		Ultradian Cycle		Circadian Trend Period
			Mean ^c	SD ^d	Amplitude ^e	Period	
Depressed group							
1	17	28	34	3.6	26	9	+26
2	11	19	34	3.1	14	3	+8
3	19	22	70	3.5	32	6	+29
4	13	21	43	2.4	10	4	+5
5	19	21	24	3.4	8	5	-23
6	14	27	51	3.6	22	4	+16
7	17	22	48	3.6	8	4	+33
8	26	35	14	3.1	22	3	-11
9	12	21	54	3.3	13	4	+15
Mean	16	24	41	3.3	17	4.7	+11
SD	4.6	5.1	17	0.39	8.6	1.8	18
Nondepressed group							
1	1	2	74	3.0	14	5	+1
2	5	12	59	2.8	6	4	-10
3	3	2	91	1.3	3	4	-2
4	2	3	83	2.6	11	4	+14
5	1	3	83	2.8	13	6	-3
6	2	2	75	1.4	2	7	+12
7	1	3	50	1.9	5	8	+27
8	0	0	77	3.5	10	6	+1
9	0	0	71	2.4	7	4	+4
Mean	1.7	3.6	74	2.4	7.9	5.3	+4.9
SD	1.6	1.2	13	0.74	4.3	1.5	11

^aSignificant difference between group means ($t=9.04$, $p<0.001$, two-tailed test; $U=18$, 0 , $p<0.001$). For all comparisons, $df=16$.

^b $t=10.2$, $p<0.001$; $U=81$, 0 , $p<0.001$.

^c $t=4.61$, $p<0.001$; $U=4$, 77 , $p<0.001$.

^d $t=3.15$, $p<0.01$; $U=71$, 10 , $p<0.01$.

^e $t=2.91$, $p<0.01$; $U=68$, 14 , $p<0.02$.

RESULTS

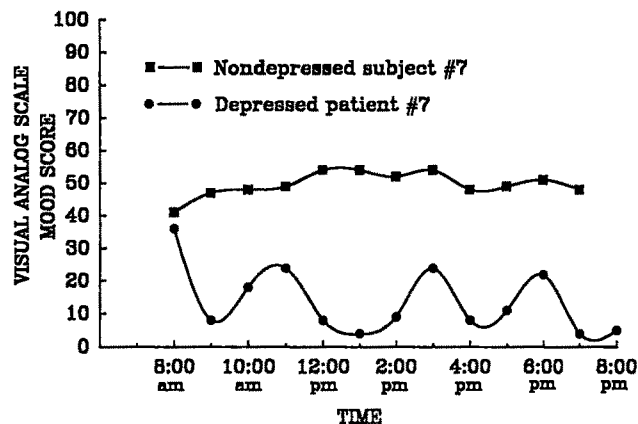
Table 1 shows that the Hamilton, Montgomery-Asberg, and visual analogue scale scores were highly consistent with the depressive diagnoses assigned to patients in the depressed group. These scales also confirmed the absence of significant depressive symptoms in the nondepressed group. Table 1 also illustrates that the depressed and nondepressed groups differed significantly on each of these indices of depression. The amount of hour-to-hour mood variability, measured as the log of standard deviation of each subject's scores, was significantly different for the two groups. Specifically, the depressed group demonstrated significantly greater mood variability during the hours of testing (table 1, column 5). Figure 2 is presented to illustrate differences in mood variability between a depressed patient and a nondepressed subject. The moods of both subjects depicted in this figure appear to vary in the pattern of an ultradian cycle; however, the depressed patient exhibits a rhythm of greater amplitude. Although all raw time series plots did not reveal such obvious ultradian cycles in mood, further analyses using complex demodulation did, indeed, reveal the presence of ultradian cycles in nearly all subjects. This is evidenced by correlation coefficients (r^2) between raw data and an ultradian model in the range of 0.85–0.99 for all subjects. In fact, 13

of the 18 subjects tested had r^2 values of 0.95 or higher.

A comparison of original data to an ultradian cycle model, obtained by complex demodulation of raw data, is presented in figure 3. Figure 3 shows raw visual analogue scale time series data for a different depressed patient, with its corresponding transformations into ultradian and circadian models. It illustrates that most of the patient's mood variability, observed as hour-to-hour visual analogue scale score changes, is accounted for by a 3-hour cycling process. By comparison, the estimated 24-hour cycle model appears to account for very little of the observed variability of mood between the hours of 8:00 a.m. and 8:00 p.m.

We found a significant difference in the amplitude of ultradian cycles ($t=2.91$, $df=16$, $p<0.01$) between the depressed and nondepressed groups (table 1). We found no significant difference between groups in length of ultradian cycle period. The range of ultradian cycle periods was 4–8 hours in the nondepressed group. There was no significant difference between groups in the ultradian cycle periods.

Finally, table 1 shows circadian trends for the two groups. As noted, no significant difference between depressed and nondepressed mean slopes was found. It is noteworthy, however, that six of nine depressed patients had relatively large positive slopes ($m[\text{slope of the line}]>10$), indicating general mood elevation over the

FIGURE 2. Raw Time Series Data on Mood Variation in a Nondepressed Subject and a Depressed Inpatient

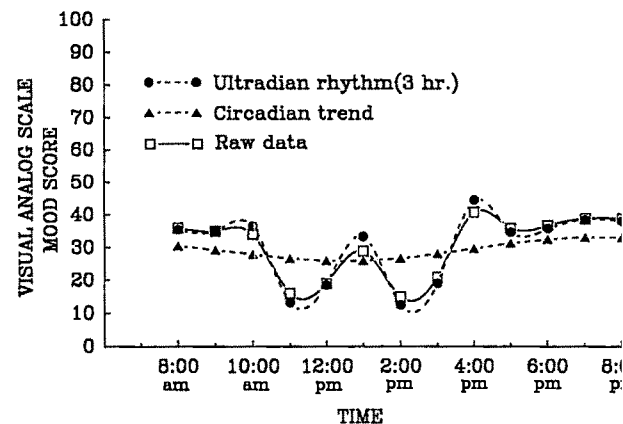
hours tested, while only three of nine nondepressed subjects demonstrated changes of this magnitude.

DISCUSSION

Before consideration of the clinical applications and theoretical implications of these findings, it should be noted that the study was limited by a small number of subjects, a sample of convenience, and moderate control of environmental stimuli. While this study revealed robust differences, replication on a larger scale is required to ensure reliability of the findings. Replications on a larger scale that include subgroup analyses for melancholia, bipolar, psychotic, and seasonal affective disorder types of depression may reveal differences in ultradian cycle characteristics for these subgroups. We share the concerns expressed in previous studies regarding the possible confounding effects of environmental stimuli (10). Although we made moderate efforts to hold environmental stimuli constant, clearly, future studies that further limit interpersonal contacts and medical treatments may permit greater detection specificity. Despite these limitations, we believe that we have illuminated several interesting aspects of depression.

The finding of 4–8 hour ultradian cycles of mood in our nondepressed subjects closely approximates an earlier report by Tsuji and co-workers (17) of 4–6 hour cycles in normal volunteers. Our finding of no significant difference in cycle period between the two groups suggests that differences in ultradian cycle amplitude, not the period, account for the greater variability of mood observed in depression. The relatively minor amplitude changes noted in two of the depressed patients, however, suggest a limit to this finding and may represent a subpopulation of depressed patients. Our observation of a large circadian trend in six of nine depressed patients is consistent with previous studies of circadian cycles (10).

Greater ultradian rhythm amplitude associated with depression, as described in this study, may present a

FIGURE 3. Ultradian Cycle, Circadian Trend, and Raw Time Series Data for a Depressed Inpatient

new dimension to theoretical explanations of the etiology of depression. Most theories addressing biological rhythms have focused on circadian cycle parameters. One review of circadian rhythm abnormalities concluded that the pathophysiology of affective disorders is related to the circadian system (i.e., suprachiasmatic nucleus and its connections) (24). Souetre et al. (25) have suggested that a blunted circadian rhythm amplitude of several measures including cortisol, melatonin, and TSH levels is the main chronobiological abnormality. One may speculate that the observed increase in ultradian rhythm amplitude might represent the increase in activity of a secondary oscillating network, which increases in amplitude in order to approach homeostatic levels of the blunted parameters.

Our findings also suggest practical applications for the clinical psychiatrist. The greater mood variance of depressed patients may require that repeated mood assessments be made over the course of the day in order to obtain an accurate impression. We recommend that repeated mood assessments be made on three to four occasions, and at unequal intervals, throughout the day. Alternatively, outpatients suspected of suffering from depression may be seen at varying appointment times. Simple repeated measures of depression, such as the Visual Analogue Mood Scale, may be administered by high-functioning patients themselves or by support staff. These repeated examinations should be done during the initial assessment period and whenever treatment changes are being considered in order to avoid comparing an ultradian cycle peak on one day to trough on a subsequent day.

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New Policy for References

Effective with the September 1991 issue, *The American Journal of Psychiatry* instituted a policy of listing the names of all authors of work cited in references. Authors of submitted manuscripts and letters to the Editor must include the surnames and initials of all authors in references. The use of "et al." is no longer acceptable.

Depression Through the First Year After the Death of a Spouse

Sidney Zisook, M.D., and Stephen R. Shuchter, M.D.

Objective: This study assesses the frequency of depressive syndromes during the first 13 months after the death of a spouse. **Method:** Men and women whose spouses had recently died were identified through death certificate records. These subjects completed a multidimensional questionnaire and were interviewed 7–8 weeks (2 months) after the death. Follow-up questionnaires were completed 7 and 13 months after the death. The questionnaires contained specific items corresponding to DSM-III-R criteria for depressive episodes as well as other widely used measures of depressive symptoms such as the Zung Depression Scale and the Hopkins Symptom Checklist. **Results:** Eighty-four (24%) of 350 widows and widowers met criteria for depressive episodes at 2 months, 72 (23%) of 308 did so at 7 months, and 46 (16%) of 286 did so at 13 months. At each time period, the prevalence was substantially higher than the 4% rate of depressive episodes observed in a comparison group of 126 subjects whose spouses were still living. Widows and widowers most likely to meet criteria for depressive episodes 13 months after the bereavement were younger, had past histories of major depression, were still grieving 2 months after the loss, and met DSM-III-R criteria for depressive episodes 2 and/or 7 months after the death. **Conclusions:** Depressive episodes are common after the death of a spouse. Clinicians should maintain a high index of suspicion for the possibility of depression, particularly in young widows and widowers who have a past history of depression or who experience a full depressive syndrome soon after the loss.

(Am J Psychiatry 1991; 148:1346–1352)

Major depressive disorders are highly prevalent (1) and are associated with substantial medical and psychosocial morbidity (2–4). Despite these factors, we still have a great deal to learn about the etiology of these disorders. A case in point relates to the role of psychosocial stress in the onset, relapse, and recurrence of major depressive disorders (5, 6). Because the death of a spouse has been considered the prototype of a severe life stressor (7) and has been associated with the onset of multiple psychiatric symptoms, including depression (8–12), it may provide an ideal model for studying the relationship of stress to major depressive disorders.

A term that is used in many different ways, “depression” can refer to a symptom, syndrome, or disorder. As a symptom of grief, depression is synonymous with sadness, a ubiquitous affect that most bereaved individuals experience from time to time, less so as the loss becomes more remote. As a grief-related syndrome, the

depression of bereavement refers to a frequently observed constellation of symptoms that may be clinically indistinguishable from major depressive disorder. Although a full depressive syndrome that fulfills all of the symptom criteria for a major depressive episode is seen in almost 50% of all widows and widowers at some time during the first year of bereavement (9), DSM-III-R considers this syndrome “uncomplicated bereavement” rather than major depressive disorder when its onset is within the first 3 months of the death.

Uncomplicated bereavement is common. In an epidemiologic survey of affective disorders in a United States urban community, Weissman and Myers (13) found a lifetime rate of grief, or uncomplicated bereavement, of 10.4% (2.7% of men and 16.2% of women). They defined “grief” as a constellation of depressive symptoms meeting criteria for major depression but appearing within 3 months of the death of a close relative. Symptoms that lasted more than a year were considered symptomatic of a major depression. However, very little information is available to help clinicians determine how often or under what circumstances the early depressive syndrome (i.e., uncomplicated bereavement) does, in fact, spontaneously resolve, versus how often it evolves into a major depressive episode. Clayton et al. (9, 14, 15) found that 35% of widows had a full depressive syndrome 1 month after the death of their spouses.

Received July 3, 1990; revisions received Dec. 18, 1990, and March 14, 1991; accepted April 14, 1991. From the University of California, San Diego, Department of Psychiatry. Address reprint requests to Dr. Zisook, 3427 Fourth Ave., San Diego, CA 92103.

Supported by National Research Service grant MH-30914 from NIMH.

The authors thank Mary Mulvihill, Ph.D., for computer and statistical consultation.

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Under our current nosology, these women would be considered to have uncomplicated bereavement. However, 17% of the widows studied by Clayton et al. (9, 14, 15) were still depressed 1 year later, and 13% were depressed for the entire year. These data would seem to indicate that between one-third and one-half of widows with uncomplicated bereavement go on to develop major depression.

The present study attempts to confirm the findings of Clayton et al. by determining the frequency of *DSM-III-R*-defined depressive syndromes over the first year after the death of a spouse and to identify risk factors for the development of major depression.

Risk factors for major depressive episodes occurring after the death of a spouse are not fully established. Our previous work (16) suggests that major depression is more likely when the surviving spouse experiences a full depressive syndrome early after the death, when there is a past personal or family history of major depressive disorder, when social supports are lacking, and when intercurrent negative life events overwhelm the already strained coping apparatus. There is also some evidence that major depressive disorders after the loss of a spouse are more frequent in women (17), younger individuals (11, 18), and those who have experienced substantial financial losses (17–19); when the death is viewed as sudden and unexpected (20, 21); and when the relationship with the deceased spouse was ambivalent or overly dependent (22). This study assesses the occurrence of depressive syndromes in widows and widowers during the first year of bereavement and evaluates the relationships between several of the features already noted (e.g., past history, early reactions, age) to the occurrence of a major depressive episode persisting beyond the first full year (i.e., at 13 months).

METHOD

The study group was gathered from all newly bereaved widows and widowers in San Diego County who could be identified by death certificates filed at the San Diego County Department of Health Services. Widows and widowers who lived within 50 miles of the project (N=2,466) were mailed a description of the study 2–3 weeks after the death and were invited to volunteer to participate by returning a postcard indicating their willingness for a home interview.

Of the 2,466 postcards, 1,028 (42%) were returned. Of the 1,028 individuals who responded, 593 (58%) said they were not interested in participating (24% of the entire mailing) and 435 (42%) said they were or might be interested (18% of the entire mailing). All 435 respondents who said "might" or "yes" were telephoned; 350 (80%) of these volunteered to participate. Seven to eight weeks after the death of their spouses, these subjects were interviewed in their own homes and completed the Widowhood Questionnaire (described later in this paper). Since no demographic data were available for the individuals who chose not to return

postcards or who said they did not wish to participate in the study, it is not possible to compare respondents with nonrespondents. However, table 1 suggests that the study group spanned a large range of ages and tended to include a disproportionate number of women, Caucasians, and highly educated individuals.

Of the 350 widows and widowers who entered the study, 308 (88%) completed 7-month follow-up questionnaires and 286 (82%) completed 13-month follow-up questionnaires. There were no differences in demographic factors, percentage of *DSM-III-R* depression, Hopkins Symptom Checklist (HSCL) (23) depression subscale scores, or Zung Depression Scale (24) scores between those who did or did not complete follow-up questionnaires. The major reasons for not completing the questionnaire at 13 months were noncompliance with questionnaire return (N=16 [25%]), moved out of the area or lost to follow-up (N=13 [20%]), deceased (N=7 [11%]), remarried (N=6 [9%]), environmental stress or too busy (N=5 [8%]), ill health (N=4 [6%]), and finding questions about the loss too painful to participate (N=3 [5%]).

Each initial evaluation session, which lasted approximately 2 hours, began with a 1-hour highly structured interview that covered, item by item, part one of the Widowhood Questionnaire. Content areas included sociodemographics; the marital relationship; the nature of the death; funeral behavior; early grief reactions; social supports and resources; present, past, and family histories of depression (*DSM-III-R* criteria) and alcoholism; and global ratings of physical health, recent work performance, and overall adjustment to the loss of the spouse. Next, the widow or widower completed part two of the Widowhood Questionnaire (16, 25), which consists of a number of self-report measures including the HSCL (23) and the Zung Depression Scale (24), as well as sets of questions assessing grief-specific feeling states, coping strategies, attachment behaviors, development of new relationships, maintenance of old relationships, changing roles and statuses, health, social and occupational functioning, and self-concepts. The research aide ensured that each item was completed as directed.

Subsequent questionnaires were mailed to each subject's home 7 and 13 months following the deaths to be completed at home and returned by mail. Each follow-up questionnaire contained a modified version of the initial part one of the Widowhood Questionnaire (deleting such items as demographics and past history) and repeat versions of part two.

Depression was measured in two ways. First, on the basis of a series of highly structured and specific items on the questionnaire, it was determined whether symptom criteria for the *DSM-III-R* diagnoses of depression were met. Thus, subjects were asked if they currently felt sad and blue and/or were anhedonic as well as whether they experienced each of the *DSM-III-R* symptoms for a major depressive episode for the better part of 2 consecutive weeks in the absence of drug or alcohol use. During the intake session 2 months after the death,

TABLE 1. Characteristics of 350 Widows and Widowers and a Comparison Group of 126 Married Subjects

Characteristic	Widows and Widowers	Comparison Group
Age (years)		
Mean	61	60
SD	10.4	13.2
Women		
N	249	86
%	71	68
Caucasian		
N	333	125
%	95	99
Protestant		
N	168	55
%	48	44
Number of years married		
Mean	32	33
SD	14.2	17.0
Number of years of education		
Mean	14.2	15.1
SD	2.6	2.6
Personal history of depression		
N	49	16
%	14	13
Family history of depression		
N	88	38
%	25	30
Religious practices		
Attended services in past month		
N	231	62
%	66	49
Number of days attended services in past month		
Mean	2.6	2.4
SD	5.3	4.9
Social supports		
Engaged in social activities in past month		
N	333	122
%	95	97
Number of days socially active in past month		
Mean	9.1	10.5
SD	7.3	7.1
Number of confidants		
Mean	2.5	3.1
SD	3.1	4.3
Health during past year		
Number of visits to physician		
Mean	6.9	6.6
SD	7.9	14.0
Hospitalized		
N	55	13
%	16	10

the research aide went over each of these questions to ensure that the widow or widower understood each item and accurately responded. The same items were included on all follow-up questionnaires. A computerized scoring program assessed whether *DSM-III-R* criteria for depressive episodes were met.

The second way depression was measured used two psychometric self-report scales for depression, the Zung Depression Scale (24) and the HSCL subscale for depression (23). Based on large community and patient population studies, the Zung total score (SDS index)

can be divided into categories of no depression and mild, moderate, or severe depression. An SDS index score of 60 or greater is considered indicative of severe depression (24).

This study also reports on a comparison group of 126 demographically similar men and women whose spouses were still living. This comparison group came from several sources: neighbors and relatives of the staff at the clinic where the project office is housed, responses from public service announcements, and requests for adult volunteers at church groups and community centers where older adults are likely to congregate. The comparison group completed a modified version of the Widowhood Questionnaire that included questions about past and present depression as well as the HSCL depression subscale and the Zung Depression Scale.

RESULTS

As described in table 1, the majority of the subjects were middle-aged to elderly women who were white, Protestant, and well educated and had been married to the deceased spouse for the better part of their adult lives. Although both widows and widowers tended to experience a decrease in their gross family incomes shortly after the loss of their spouse, the loss of income was significantly more frequent for widows (76% [N=189] versus 47% [N=47], $\chi^2=26.6$, $df=1$, $p<0.001$). The married comparison group was similar to the group of widows and widowers on all demographic and past history variables, including personal and family history of depression, number of days attending church in the past month, number of days with social activities in the past month, and number of confidants.

Past Relationship, Type of Death, and Grief Reactions

In general, most of the survivors described their marital relationships in positive terms: 231 (66%) rated it as very good, 231 (66%) as very close, 228 (65%) as very loving, 249 (71%) as very supportive, and 212 (61%) as very comfortable. Each of these ratings was based on a 4-point scale on which 1=very close, 2=close, 3=distant, and 4=very distant. Only 22 (6%) of the subjects had been widowed previously, and 90 (26%) had been divorced one or more times. About two-thirds of the spouses (N=221) had died after a prolonged illness (longer than 3 months); the remainder (N=125) died suddenly, including three by accidents and eight by suicide (data were not available for two subjects, and "other" was listed by two subjects).

Two hundred five (59%) subjects stated that they began grieving before the death; 28 (8%) felt their grieving was complete by the end of the second month, and 177 (51%) felt they were still grieving. Another 140 (40%) of the subjects stated that their grieving began after the death; only 10 (3%) subjects felt their grieving was complete 2 months after the death, and 130 (37%)

TABLE 2. Factors Significantly Associated With *DSM-III-R* Major Depressive Episodes 13 Months After the Death of a Spouse in 286 Widows and Widowers

Factor	N	Subjects Who Were Depressed		Subjects Who Were Not Depressed		Analysis	
		N	%	N	%	χ^2 ^a (df=1)	p
Age (years)	286					5.6	<0.05
65 or younger	190	38	20	152	80		
Older than 65	96	8	8	88	92		
Personal history of depression	281					14.4	<0.001
Positive	35	14	40	21	60		
Negative	246	32	13	214	87		
Grief resolution at 2 months	285					5.4	<0.05
Still grieving	254	46	18	208	82		
Grieving ended	31	0	0	31	100		
Depression at month 2	286 ^b					5.3	<0.05
Depressed	66	22	33	44	67		
Not depressed	220	24	11	196	89		
Depression at month 7	275 ^b					7.2	<0.01
Depressed	62	27	44	35	56		
Not depressed	213	15	7	198	93		
Physical health	270					15.1	<0.001
Poor-fair	61	20	33	41	67		
Good-excellent	209	23	11	186	89		

^aYates' continuity correction used.^bMcNemar's chi-square used because the analysis is a repeated-measures design.

considered themselves to be still grieving. Three (1%) of the subjects reported not grieving at any time. Thus, the majority of subjects (N=307 [88%]) reported themselves still grieving at 2 months.

Depression

Thirty subjects met full *DSM-III-R* symptom criteria for depressive episodes immediately after the death of their spouses but were no longer depressed by the end of 2 months. At the end of the second month of bereavement, 84 (24%) of the 350 subjects met *DSM-III-R* symptom criteria for depressive episodes. At 7 months, 72 (23%) of 308 subjects met these criteria. After 1 full year of bereavement (13 months), 47 (16%) of 286 subjects had *DSM-III-R* major depression. Only five (4%) of the 126 subjects in the comparison group, however, met *DSM-III-R* criteria for depressive episodes at the time of their evaluations.

Using a cutoff score of 60 or more on the SDS index of the Zung Depression Scale (24), we found that 105 (30%) of the 350 bereaved spouses were severely depressed at 2 months (mean±SD total score=49.97±12.69), 68 (22%) of 308 subjects did so at 7 months (mean total score=49.99±12.29), and 51 (18%) of 286 subjects did so at 13 months (mean total score=47.67±12.25). Only four (3%) of the married comparison subjects had SDS indexes of 60 or more (mean total score=39.22±8.77). At each time period, there was a significant association between depression defined by the SDS index and by *DSM-III-R* (e.g., at 13 months, $\chi^2=29.97$, df=1, $p<0.001$).

As with the *DSM-III-R* classification and Zung scores, the HSCL depression subscale scores also gradually declined over the first year but remained substan-

tially higher among the widows and widowers (1.79±0.55 at 2 months, 1.75±0.56 at 7 months, and 1.62±0.52 at 13 months) than among the married comparison subjects (1.16±0.22). At all time points, the HSCL depression scores also were significantly associated with *DSM-III-R* ratings (e.g., at 13 months, $r_s=0.5093$, $p<0.001$), and with total Zung scores (e.g., at 13 months, $r=0.7238$, $p<0.000$).

Factors Related to Depression at 13 Months

Table 2 lists the factors that had statistically significant relationships with *DSM-III-R* depression at 13 months. The only demographic factor related to *DSM-III-R* depression at 13 months was age. The mean age of the 46 subjects with depression was 57±9.95 years, compared with a mean of 62±9.61 years in the 240 nondepressed widows and widowers ($F=10.62$, df=1, 281, $p<0.001$). In addition, subjects older than 65 years of age were significantly less likely to be depressed than younger subjects (table 2). A past personal history of depression was significantly related to depression, but family history was not. Neither religious practices, social supports, quality of the past marital relationship, or type of death was significantly related to depression. On the other hand, those widows and widowers who were still grieving at 2 months or were depressed at either 2 or 7 months were more likely to be depressed at 13 months. It is especially notable that not a single widow or widower who felt that his or her grieving had ended at 2 months was depressed at 13 months. Finally, depression was associated with poor physical health. Further univariate analyses revealed that each of the factors that was significantly related to *DSM-III-R* depression was also significantly related to scores on the

HSCL depression subscale. In addition, a positive family history for depression ($F=11.93$, $df=1$, 281, $p<0.001$) and a self-rated lack of satisfaction with social supports ($F=13.48$, $df=1$, 281, $p<0.001$) were also related to HSCL depression at 13 months.

DISCUSSION

This study examined the relationship between depression and the death of a spouse during the first year of bereavement. Three major findings emerged. First, full depressive episodes, as defined by *DSM-III-R*, are common throughout the first year after the death of a spouse. Second, the depressive episodes may occur not only in the early months of bereavement but later as well. Third, individuals who appear to be at highest risk for having depressive episodes 13 months after their loss are younger widows and widowers, have past histories of depressive episodes, are still grieving 2 months after the loss, experience depressive episodes 2 and/or 7 months after the loss, and perceive themselves as being in poor physical health.

Before further discussing the findings, we should address several methodological limitations that affect the study's generalizability. First, the study group was not a totally random or unbiased sample. Indeed, only about 34% of the bereaved spouses who responded to our initial mailing ultimately enrolled in the study, and we were unable to compare those who participated in the study with those who did not. Most of the subjects in the group studied were white, middle-class, and well educated, and their responses to the stress of bereavement might be different from those of other groups. Of the 350 bereaved spouses who began the study, only 286 (82%) completed all three depression ratings. Although this dropout rate may have biased the 13-months results, the dropouts were not significantly different from the subjects who continued to participate in demographic variables or in the percentage of subjects with depressive episodes at either of the first two rating periods.

Another limitation is that the validity and reliability of the Widowhood Questionnaire have not yet been tested, although some of the scales used, such as the Zung Depression Scale and the HSCL depression subscale, have been studied extensively and are relative gold standards for self-rated assessments of depressive symptoms. In this regard, it should be noted that the *DSM-III-R* diagnoses were significantly associated with depression as measured by the Zung Depression Scale and the HSCL depression subscale. Finally, an ideal comparison group would be one recruited and enrolled just as the experimental group was and would have been reevaluated at the same intervals as the widows and widowers. However, the married comparison group did match well with the experimental group on all relevant variables and likely provides a reasonable backdrop against which the affective states seen after the death of a spouse can be evaluated.

Despite these caveats, the study strongly suggests that depressive episodes are more frequent in widows and widowers than in men and women whose spouses are still alive. In terms of the frequency of depressive episodes, our results are strikingly similar to those of Clayton et al. (9, 14, 15), who found rates of 35% 1 month after the loss (as opposed to our 33% at or before 2 months), 25% at 4 months (as opposed to our 23% at 7 months) and 17% at 13 months (as opposed to our 16%). Although the rates of depression in both of these studies are high, they are considerably lower than those published in a recent study by Jacobs et al. (26), who found *DSM-III-R* depression present in 32% of bereaved spouses at 6 months and 27% at 12 months. These higher rates may be accounted for by the fact that the Jacobs study selected subjects who either had depression or were worried about getting depressed and used brief telephone interviews for assessment. Criteria for depression were similar in all three studies, although Clayton (9) used Feighner diagnostic criteria, a forerunner of *DSM-III-R*. Neither Clayton nor Jacobs et al. studied nonwidowed comparison subjects.

In our study, the rate of depressive episodes among the widows and widowers at each time point was considerably higher than the 4% rate found in the comparison group or the 2% 6-month prevalence rate for major depression found in the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area study, which used the NIMH Diagnostic Interview Schedule and *DSM-III-R* for diagnosis (1, 27).

Although depressive syndromes are found most frequently early in the course of bereavement, they may occur at any time throughout the first year. Indeed, in our study group the rate of depression was almost identical 2 and 7 months after the loss and remained well above the rate among the comparison subjects, even after the first year. *DSM-III-R*, in differentiating uncomplicated bereavement from major depression, states that the depressive syndrome seen in the former should occur early (within the first 2 to 3 months) and should not be prolonged. Although *DSM-III-R* states that "the duration of 'normal' bereavement varies considerably among different cultural groups," it does not specify an upper limit. Thus, it is likely that the subjects in our study group who met criteria for depressive episodes at 13 months (16% of those who completed the questionnaire) had major depressive disorders and required active treatment; it is less clear how many of the other depressive episodes, especially those seen at 7 months, might also have represented major depressive disorder. Many of the depressive episodes seen after the loss of a spouse, then, appear to be persistent and are more like an illness than the label of "uncomplicated bereavement" connotes. *DSM-III-R*'s guidelines, falling short of research-validated operational criteria, do not fully clarify this complex issue, and clinicians may find it difficult to differentiate uncomplicated bereavement from major depressive disorder. Since diagnosis ideally leads to treatment and prognosis, this diagnostic confusion may have important clinical implications. We plan to

address these diagnostic issues more fully in a separate communication.

One of the long-range goals of the San Diego Widowhood Project is to develop treatment strategies based on a sound understanding of the natural history and course of bereavement. A number of treatment modalities have been evaluated, including self-help (28), dynamic (29), supportive (30), and group (31) psychotherapies, but none of these is specifically geared to treat or prevent depression in the bereaved. To date, only one report on the potential utility of antidepressant medications has been published (32), but this study was uncontrolled and included only widows and widowers depressed for at least 6 months. The results of this study point to the importance of learning whether early psychotherapy and/or psychopharmacological interventions for widows and widowers at high risk for depression might help prevent or ameliorate prolonged depressions, but, clearly, controlled prospective studies are needed.

We have previously looked at factors associated with depression 2 months after the loss of a spouse (16). However, since it is not clear whether these "depressive syndromes" represent major depressive disorders or uncomplicated bereavement, the relevance of these findings is unclear. On the other hand, factors related to depressive episodes 13 months after the loss might bear a more precise and meaningful relationship to the pathophysiology of depression. Several features of the bereaved husband or wife—their past history of depression and their early reactions to the loss—were associated with having depressive episodes 13 months after the loss. Of the demographic factors studied, only age emerged as significantly related to depressive episodes at 13 months. Although clinical impressions suggested that the elderly were at greatest risk for depression, more recent epidemiologic studies have found otherwise (1, 33). Similarly, although some studies have found elderly bereaved spouses to be at greatest risk for depression, most, like the present study, have found young widows and widowers to be at highest risk for depression (11, 12, 14). That other demographic factors, such as gender, were not related to depressive episodes, is not surprising, because Clayton et al. (9, 34) have found that an equal risk between widows and widowers is one of the distinguishing features of what they referred to as the "depression of widowhood," in contrast to primary depressive disorders, which are more frequent in women.

We also found that a past history of depression was related to the presence of depressive episodes 13 months after bereavement, a finding that may be compatible with common sense but has not been found consistently in previous studies (26, 35). Indeed, although Clayton was not able to find that a past history of depression increased the likelihood of responding to the death of a spouse with depressive episodes (9), she did find that the presence of a preexisting psychiatric illness (including depression) was associated with the persistence of the depressive syndrome from the first to the 13th month

after the loss (36). We think that other studies have not found more of a relationship between a past history of depression and the "depression of widowhood" because the relatively small numbers of subjects in those studies have not provided adequate power to find the relationship. In any case, it comes as no surprise that one's response to a stressful life event is related to one's past history and unique vulnerabilities.

Like several other investigators (9, 26), we did not find a family history of major depression to be associated with *DSM-III-R*-defined depressive episodes at 13 months, although we had previously found family history to be related to depressive episodes at 2 months (16). In this study we found family history to be related to depressive symptoms (as indicated by HSCL depression subscale scores) but not to depressive episodes (as defined by *DSM-III-R* criteria) at 13 months. It may be that a family history of depression is an important predisposing factor for early depressive syndromes or for depressive symptoms but that it is not as virulent a risk factor as a past personal history of depression when it comes to major depressive episodes.

Perhaps the best predictor of depressive episodes at 13 months is evidence for earlier active grief and depression. Many of us have been taught to believe that early intense grief is the normal and healthy response to loss and that it tends to protect us from later depression (37), but empirical findings more often have suggested that intense early reactions may be associated with intense later reactions, such as chronic grief (22), unresolved grief (38), or depression (39). In this study, we found that none of the 31 widows and widowers who reported no grief at 2 months was depressed 11 months later. On the other hand, 18% of those who were still grieving at the end of 2 months were depressed at 13 months. Similarly, we found that depressive episodes at 2 months as well as depressive episodes at 7 months were both strongly related to depressive episodes 13 months after the death of a spouse. Clayton (36) also found early depressive syndromes to be significantly associated with a depressive syndrome 13 months after the loss of a spouse. Thus, responding to a stressful life event with depressive symptoms may be a forerunner to the later development of a depressive disorder; early responses may be a window through which persistent psychopathology can be previewed.

In summary, depressive episodes are common after the loss of a spouse and, for many widows and widowers, may be relatively persistent. Among factors most related to depressive episodes at 13 months are younger age, a past history of major depression, still actively grieving at 2 months, and experiencing depressive episodes at 2 and/or 7 months. *DSM-III-R* attempts to define and differentiate uncomplicated bereavement, a syndrome supposedly requiring no specific medical attention or treatment, from major depression, but the distinctions it offers are not always helpful. Because not only depressive disorders but even depressive symptoms are so debilitating and may be associated with substantial morbidity and mortal-

ity (2, 3), the depressions associated with the loss of a spouse are a clinically important area of inquiry, and further study is warranted in this relatively untapped field.

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Predictors of Relapse Into Major Depressive Disorder in a Nonclinical Population

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Objective: This study sought to describe the natural history of major depressive disorder in a large group of nonclinical subjects. In particular, the analysis determined demographic and clinical risk factors for the recurrence of major depressive disorder. **Method:** Relatives, comparison subjects (matched to relatives for age and sex), and spouses of affectively ill probands underwent structured clinical assessments before and after a 6-year interval. **Results:** Of 396 individuals who had had only major depressive disorder that ended before the initial evaluation, 33.8% (N=134) developed a new episode during the 6-year follow-up period. Youth, but not sex, was an important demographic risk factor. The presence of minor depression at the time of initial evaluation and the number of symptoms recalled from the worst previous episode were additional clinical risk factors. At the initial evaluation, 200 other subjects had described a previous history of both major depressive disorder and a nonaffective mental disorder. When compared to the subjects who recalled only a history of major depressive disorder, these subjects were more likely to have been in an episode of chronic intermittent depression at the initial evaluation and to recall a greater number of episodes as well as a greater number of symptoms in the worst episode. A history of a nonaffective mental disorder significantly increased the risk of relapse into major depressive disorder. **Conclusions:** These findings agree well with a recent review of clinically based follow-up studies. Thus, youth and a history of nonaffective illness are important risk factors for the recurrence of major affective disorder in a broad variety of settings.

(Am J Psychiatry 1991; 148:1353-1358)

The psychiatric literature presents a biased picture of major depressive disorder and its natural history. First, almost all efforts to study the course of affective disorder have described subjects who sought treatment for active illness. Second, since most researchers have had their headquarters at tertiary medical centers, the sample of patients available to them has been biased toward individuals with relatively recurrent and disabling illnesses. Finally, because these follow-ups began with actively ill subjects, analyses have usually focused on the length of index episodes and the predictors of recovery from those episodes. The study of relapse requires longer observation periods, and even then the observed events are biased toward those that occur sooner rather than later. Thus, most studies have lacked

the range to describe fully the risks for relapse, and almost all have been restricted to subjects with relatively severe illness. The study we describe avoided these problems.

As part of the National Institute of Mental Health (NIMH) Collaborative Study Program on the Psychobiology of Depression—Clinical Studies family substudy, the relatives and spouses of affectively ill probands and a group of comparison subjects matched to a subset of the relatives were evaluated for lifetime psychiatric disorders. The reevaluation of these individuals 6 years later provided a follow-up of a large, nonclinical population. Among subjects with no prior history of major depressive disorder, youth (age less than 40 years), female sex, and a history of nonaffective mental disorder were each powerfully and independently associated with a high probability of prospectively observed major depressive disorder (1). Additional risk factors operating among women were marital disruption, residence in a farm setting, and high educational achievement. We sought to determine whether these same, or other, factors would predict the recurrence of major depressive disorder in a nonclinical but previously depressed subject group.

Received Oct. 30, 1990; revision received March 14, 1991; accepted April 22, 1991. From the National Institute of Mental Health Collaborative Program on the Psychobiology of Depression—Clinical Studies. Address reprint requests to Dr. Coryell, Department of Psychiatry, University of Iowa College of Medicine, 500 Newton Rd., Iowa City, IA 52242.

This manuscript has been reviewed by the Publication Committee of the Collaborative Program and has its endorsement.

TABLE 1. Demographic Data at Intake on 596 Subjects With Histories of Major Depressive Disorder Who Were Reevaluated 6 Years Later

Variable	History of Major Depression Only (N=396)		History of Major Depression and Nonaffective Disorder (N=200)	
	N	% ^a	N	% ^a
Female sex ^b	302	76.3	108	54.0
Marital status				
Never married	68	17.7	44	23.5
Married	239	62.2	110	58.8
Divorced or separated	49	12.8	28	15.0
Widowed	28	7.3	5	2.7
Educational status				
Graduate or professional degree	34	8.7	17	8.6
Bachelor's degree	74	18.9	28	14.1
Some college	113	28.8	52	26.3
High school graduate	113	28.8	66	33.3
Some high school	36	9.2	25	12.6
Junior high school	19	4.9	8	4.0
Less than 7 years	3	0.8	2	1.0
Occupational status				
1 (high-level executive or equivalent)	16	4.1	11	5.6
2	75	19.2	22	11.2
3	75	19.2	37	18.9
4	92	23.6	48	24.5
5	44	11.3	32	16.3
6	39	10.0	19	9.7
7 (unskilled employee or equivalent)	13	3.3	9	4.6
8 (expected wage earner who never worked)	—	—	—	—
9 Other (student, housewife)	36	9.2	18	9.2
Residential area				
City	155	45.5	81	49.1
Town	48	14.1	21	12.6
Suburb	114	33.4	54	32.3
Rural, nonfarm	10	2.9	6	3.6
Rural, farm	14	4.1	4	2.4

^aNs on which %s are based vary because of missing data on some items for some patients.

^bSignificant difference between groups ($\chi^2=30.7$, $df=1$, $p=0.0001$).

METHOD

The NIMH Collaborative Program on the Psychobiology of Depression—Clinical Studies included a family study (2) of 616 probands with major depressive disorder, schizoaffective disorder, or mania according to the Research Diagnostic Criteria (3). Raters blind to proband diagnosis interviewed all willing first-degree relatives over the age of 17 as well as all spouses of the probands. They also evaluated, as community comparison subjects, age- and sex-matched acquaintances of a randomly selected subgroup of the relatives. Because the study design intended the rates of illness among comparison subjects to approximate community rates, it did not exclude those with past or present psychiatric disorders.

Initial evaluations included use of the Schedule for

Affective Disorders and Schizophrenia (SADS) (4) and the Personal History of Depressive Disorders. The former instrument generated diagnoses according to the RDC, and the latter listed demographic details.

Study personnel recontacted the relatives, spouses, and comparison subjects 6 years after the initial evaluation. A modification of the lifetime version of the SADS, the Schedule for Affective Disorders and Schizophrenia—Interval (SADS-I) focused on psychopathology during this 6-year interval. Raters dated the beginning and end of each new episode and determined the quality of symptoms, the impact on functioning, the treatment received, and overall severity as reflected in the Global Assessment Scale (GAS) (5) score.

Altogether, 3,119 subjects underwent initial evaluations. Of these, 1,319 were considered to have been never ill; they had no history of a specific RDC disorder or of any other disorder which, in the raters' judgment, would have met the *DSM-III* criteria for an axis I or axis II disorder. There were also 329 nonaffectively ill subjects who had no history of major depressive disorder when initially evaluated but who had had a past or present diagnosis of any of the disorders listed in the RDC under the definition for secondary depression. An earlier report (1) described the demographic and symptom predictors of the first onset of major depressive disorder among the previously never-ill subjects and among those with a history of one or more nonaffective disorders.

Still other subjects had had a previous history of major depressive disorder although they were not in a current episode when initially evaluated. Of these, 536 had had only major depressive disorder, with or without other affective diagnoses. Another 288 had had, in addition, one of the listed nonaffective disorders. These included alcoholism (N=119), phobic disorder (N=49), drug use disorder (N=44), panic disorder (N=21), antisocial personality (N=6), obsessive-compulsive disorder (N=5), preferential homosexuality (N=3), schizoaffective disorder (N=2), somatization disorder (N=2), schizophrenia (N=1), and organic brain syndrome (N=1). Any relapse in this latter group of 288 would have met the criteria for RDC secondary major depressive disorder, while any relapse in the former group of 536 would have been considered a primary major depressive disorder.

RESULTS

Demographic data at intake on the 596 subjects with histories of major depressive disorder who were evaluated 6 years later are shown in table 1. In addition to a significant difference in percentage of female subjects between the group with depression only and the group that also had nonaffective disorder, there was a significant difference in age between the two groups: mean \pm SD=39.8 \pm 14.2 years for the subjects with major depressive disorder only and 35.7 \pm 11.9 years for those with major depressive disorder and nonaffective disorder ($t=3.6$, $df=594$, $p=0.0004$).

TABLE 2. Clinical Characteristics at Intake of 596 Subjects With Histories of Major Depressive Disorder Who Were Reevaluated 6 Years Later

Variable	History of Major Depression Only (N=396)		History of Major Depression and Nonaffective Disorder (N=200)	
	N	%	N	%
Other affective disorders present at intake				
Minor depressive disorder	15	3.8	3	1.5
Chronic intermittent depressive disorder ^a	23	5.8	21	10.5
Hypomanic disorder	3	0.8	4	2.0
Previous episodes of other affective disorders				
Minor depressive disorder ^b	54	13.6	11	5.5
Hypomanic disorder	43	10.9	28	14.0
Manic disorder	12	3.0	10	5.0
More than one previous episode of major depression ^{c,d}	145	36.6	95	47.5

^aSignificant difference between groups ($\chi^2=4.3$, $df=1$, $p=0.04$).

^bSignificant difference between groups ($\chi^2=9.0$, $df=1$, $p=0.003$).

^cSignificant difference between groups ($\chi^2=6.5$, $df=1$, $p=0.01$).

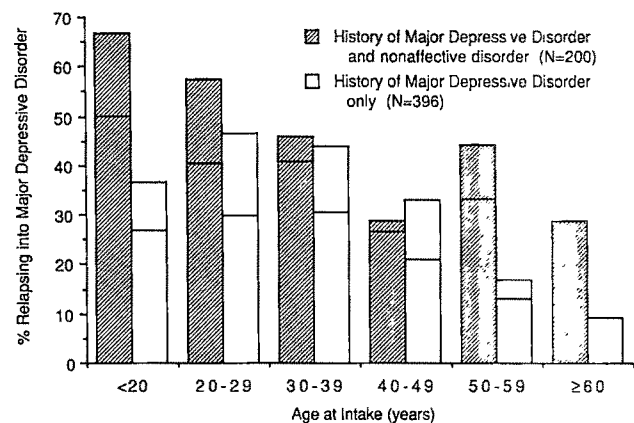
^dMean \pm SD number of episodes = 4.1 ± 13.6 for major depression only and 6.8 ± 20.4 for depression plus affective disorder (Kruskal-Wallis $\chi^2=6.7$, $df=1$, $p=0.01$). Mean \pm SD number of symptoms in worst episode = 5.3 ± 1.5 for major depression only and 5.6 ± 1.6 for depression plus affective disorder ($t=2.4$, $df=593$, $p=0.02$).

Subjects With Past Major Depressive Disorder Only

Of the 536 subjects who at intake gave a history of previous major depressive disorder and no history of the listed nonaffective disorders, 396 (73.9%) were reevaluated 6 years later. Those who completed follow-up did not differ significantly from those who did not on any of the variables listed in table 1. Among the variables listed in table 2, completers were more likely than noncompleters to have ever had minor depression (13.6%, $N=54$ of 396, and 5.7%, $N=8$ of 140, respectively; $\chi^2=6.3$, $df=1$, $p=0.01$), but a history of multiple major depressive episodes was more common among noncompleters (47.9%, $N=67$ of 140, for noncompleters; 36.6%, $N=145$ of 396, for completers; $\chi^2=5.5$, $df=1$, $p=0.02$).

One-third (33.8%, $N=134$) of the 396 subjects who completed follow-up had developed at least one episode of major depressive disorder, and 23.5% ($N=93$) had had at least one episode that met the criteria of Gershon et al. (6) for observable, major life role impairment. These rates were substantially higher than those for subjects who had had no history of mental disorder at intake (1). Of these latter subjects ($N=965$), 11.8% ($N=114$) had developed major depressive disorder (comparison with subjects who had a previous history of major depressive disorder, $\chi^2=105.9$, $df=1$, $p<0.0001$), and only 8.2% ($N=79$) had developed major depressive disorder with observable, major life role impairment (comparison with subjects who had had previous major depressive disorder, $\chi^2=50.0$, $df=1$, $p<0.0001$). On the other hand, the risk for major depressive disorder among subjects with previous primary depression approximated that for subjects who had had a previous history of nonaffective disorder only (29.0%, $N=62$ of 214).

Men had somewhat lower risks for relapse during follow-up than did women: the rates were 25.5% ($N=24$ of 94) and 36.4% ($N=110$ of 302), respectively (non-

FIGURE 1. Relation Between Age at Intake and Relapse Into Depression During 6-Year Follow-Up of 596 Subjects With Histories of Major Depressive Disorder^a

^aLines across bars indicate the percentages of subjects who relapsed into major depressive disorder with manifest impairment in the major life role. All subjects aged 60 and over who relapsed had this level of impairment.

significant difference). Moreover, a series of logistic regression analyses revealed no effects on the likelihood of relapse for interactions between sex and any of the tested risk factors listed in table 1. In subsequent analyses we therefore pooled the data for men and women.

Age was a significant determinant of risk for relapse (logistic regression $\chi^2=16.0$, $df=1$, $p=0.0001$) (figure 1): a new episode of major depressive disorder developed in 44.4% ($N=95$) of the 214 subjects under 40 years of age but in 21.4% ($N=39$) of the 182 subjects over 40 years old. Rates fell somewhat for subjects in their fourth decade, then dropped sharply for those in their 50s, and dropped again for those in their 60s. This last group had a relapse rate approximately one-fifth of that for subjects who began follow-up when younger than 40 years. These patterns held for both sexes.

TABLE 3. Relapse Into Major Depression During 6-Year Follow-Up of Subjects With Histories of Major Depressive Disorder and Nonaffective Disorder

Diagnosis	N	Subjects Who Relapsed	
		N	%
Primary major depression only	396	134	33.8
Alcoholism	119	52	43.7 ^a
Phobic disorder	49	26	53.1 ^b
Drug use disorder	44	25	56.8 ^c
Panic disorder	21	11	52.4

^aSignificantly greater than the rate for subjects with primary major depression only ($\chi^2=4.0$, $df=1$, $p=0.05$).

^bSignificantly greater than the rate for subjects with primary major depression only ($\chi^2=7.0$, $df=1$, $p=0.008$).

^cSignificantly greater than the rate for subjects with primary major depression only ($\chi^2=9.1$, $df=1$, $p=0.003$).

Relapse rates varied significantly by marital status ($\chi^2=14.7$, $df=3$, $p=0.002$). Most likely to relapse were single subjects (51% of 68), followed by those who were married (31.8% of 239), those who were divorced or separated (22.5% of 49), and those who were widowed (21.4% of 28). The single subjects were younger, however, and marital status was no longer a predictor when entered into a logistic regression analysis with age.

Of the 23 subjects with chronic intermittent depressive disorder at intake, 52.2% ($N=12$) relapsed during follow-up; 32.7% ($N=122$) of those without this disorder relapsed during follow-up. This difference approached statistical significance ($\chi^2=3.7$, $df=1$, $p=0.06$). The presence of minor depression at intake doubled the risk for relapse, and this difference was highly significant (66.7%, $N=10$, of 15 with minor depression versus 32.5%, $N=124$, of 381 without minor depression; $\chi^2=7.5$, $df=1$, $p=0.006$). In contrast, neither a lifetime diagnosis of manic disorder nor a lifetime diagnosis of hypomania increased the likelihood of relapse into major depression.

Subjects with multiple previous episodes of major depressive disorder were not significantly more likely to relapse (38.6%, $N=56$ of 145) than were subjects with only one episode before intake (31.1%, $N=78$ of 251). However, the risk for relapse did increase with the number of criterion symptoms recalled for the worst previous episode. Subjects who went on to relapse recalled a mean \pm SD of 5.6 ± 1.4 symptoms for their worst episode, whereas subjects who did not relapse recalled 5.2 ± 1.5 ($t=2.7$, $df=393$, $p=0.007$). Relapse rates were 17.4% ($N=8$ of 46) for subjects who recalled only three symptoms for their worst episode, 26.1% ($N=24$ of 92) for those who recalled only four, but 39.3% (101 of 257) for those who recalled five or more.

The four variables significantly associated with risk of relapse in the univariate comparisons were entered into a logistic regression analysis. After statistical control for the other three variables, younger age ($\chi^2=14.8$, $df=1$, $p=0.0001$), a greater number of symptoms in the

worst major depressive episode ($\chi^2=6.7$, $df=1$, $p<0.001$), and the presence of minor depressive disorder at intake ($\chi^2=5.7$, $df=1$, $p<0.02$) remained significant predictors, whereas marital status did not ($\chi^2=0.5$, $df=1$, $p=0.46$).

Subjects With Past Major Depressive Disorder and Nonaffective Disorder

Of the 288 subjects who gave a history at intake of both major depressive disorder and one of the listed nonaffective disorders, 200 (69.4%) completed the 6-year follow-up. Completers and noncompleters did not differ significantly on any baseline demographic variables.

The sex ratio for these subjects was nearly even, in marked contrast to the predominance of women among the subjects with previous primary depression only (table 1). Subjects with a history of both affective and nonaffective disorders were also significantly younger than those with only previous depression, they had had a significantly greater mean number of previous episodes, their worst episodes had featured more criterion depressive symptoms, and they were more likely to have had chronic intermittent depression at intake but less likely to have had a history of minor depression.

These subjects had a risk for relapse of 47.0% ($N=94$ of 200), a risk significantly higher than that for subjects with a history of primary depression only ($\chi^2=9.7$, $df=1$, $p=0.002$). This difference was enhanced somewhat when life role impairment was required in the definition of major depressive disorder: 36.5% ($N=73$) of those with a previous nonaffective disorder but 23.5% ($N=93$) of the 396 with primary depression only met this criterion ($\chi^2=11.2$, $df=1$, $p=0.001$). Each of the more common nonaffective disorders (present in at least 10 subjects) was important in raising the risk for relapse (table 3).

Men and women had nearly equal risks for a new episode of major depressive disorder: 47.8% ($N=44$ of 92) and 46.3% ($N=50$ of 108), respectively. Age was also not significantly associated with the likelihood of relapse (logistic regression $\chi^2=2.7$, $df=1$, $p=0.10$) (figure 1). This stood in marked contrast to the robust relation between age and relapse for the individuals without nonaffective illness.

As was the case among subjects who had never been ill, those who had previously had only nonaffective illness (1), and those who had had only major depressive disorder, subjects with a history of both major depressive disorder and nonaffective illness who were also single were at highest risk for major depressive disorder during follow-up: 63.6% ($N=28$ of 44) developed depression, compared to 42.7% ($N=61$ of 143) of the other subjects (married, divorced, separated, or widowed) ($\chi^2=5.9$, $df=1$, $p<0.03$). Again, though, the relation of single marital status to risk for relapse was no longer significant when age was taken into account, even though age itself was not a significant risk factor. None of the other demographic features tested (listed in table 1) significantly predicted relapse in this group.

Clinical history had predictive significance. Those who relapsed were much more likely to have had a history of recurrence: 60.6% (N=57) of the 94 who relapsed had had more than one previous major depressive episode, compared to 35.9% (N=38) of the 106 who did not relapse ($\chi^2=12.3$, $df=1$, $p=0.0001$). Subjects who relapsed also had a greater mean \pm SD number of depressive symptoms during the worst episode before intake (5.9 ± 1.6) than those who did not relapse (5.4 ± 1.6) ($t=2.2$, $df=198$, $p=0.03$). Relapse occurred in 33.3% (N=6) of the 18 who recalled having had three symptoms, in 42.5% (N=17) of the 40 who recalled having four symptoms, and 50.0% (N=71) of the 142 who recalled having five or more symptoms. On the other hand, current or previous episodes of minor depression, hypomania, or mania did not increase the risk for relapse among these subjects.

DISCUSSION

One in three subjects with a history of primary depression experienced at least one recurrence in a 6-year period, a risk three times that for subjects who had recalled no previous psychiatric illness at intake (1). This figure may seem high for several reasons. First, unlike most follow-up studies, this one did not begin in an index episode. Some individuals had recently been depressed, but many others had been depressed only in the distant past. Considerable evidence shows that risk of recurrence is greatest during the first 6 months after recovery (7, 8). Second, most samples that are used to characterize natural history have been collected at referral centers, and the health care system ensures that chronic or frequently relapsing patients are overrepresented at such centers. The subjects described here occupy the milder end of the severity spectrum, and their rates of recurrence should be correspondingly lower than those seen in clinically based samples. And in fact they were. In a recent follow-up of 471 probands who had recovered from an index episode of nonbipolar major depressive disorder, over 60% had relapsed by the end of a 2-year period (9).

Sex was a major determinant of onset, both for previously never-ill subjects and for those with previous nonaffective illness (1). In contrast, sex was relatively unimportant as a predictor of recurrence. Apparently, whatever factors operate to provide higher rates of depression among women do not persist beyond the first episode to promote disproportionate rates of recurrence.

Youth predicted onset for never-ill and nonaffectively ill subjects (1). Similarly, younger individuals with a history of depression only had a higher risk of recurrence. Subjects under 40 years of age were more than twice as likely as those in their 50s and five times as likely as those aged 60 or more to relapse. Thus, risk for both onset and recurrence declined markedly with age. This may seem counterintuitive in light of clinical experience. For instance, individuals over age 40 were well represented in the proband sample of hospitalized

patients: 41.9% of that sample were over 40 years of age and 14.5% were over 60 (unpublished data). It must be remembered though, that the subjects in this nonclinical sample had relatively benign illnesses and that the elderly who develop depression may be more likely to develop a chronic and disabling course. They might then be overrepresented in samples drawn from tertiary care centers.

A history of nonaffective disorder markedly increased the risk for major depressive disorder among individuals who had never previously been depressed (1). The present analysis shows that such a history also increases the risk for recurrence; nearly one-half of these individuals developed an episode during the 6-year period. Moreover, each of the more common nonaffective illnesses has this effect to an equivalent degree. Since aging did not substantially decrease risk in this study group, the additional risk of recurrence associated with nonaffective illness was particularly striking among older individuals.

Should such prevalent conditions be labeled with the same term used to designate more severe and presumably less prevalent conditions familiar to clinicians? This question of "caseness," the threshold between normal variation and disease, is an old one, and many years of investigation have yielded no clear evidence of discontinuity within the severity spectrum. Thus, there are no obvious or empirically derived thresholds with which to separate pathological or "real" depression from conditions that might be better considered normal responses to stress. In this light, we must emphasize that very common conditions are no less diseases because of their prevalence. A lifetime history of the common cold is essentially universal, yet this condition is unarguably a disease. Moreover, of the two illnesses, depression clearly has the more profound potential consequences. Given this, and the lack of a generally accepted lower limit for symptom severity, all major depressive disorder should be provisionally viewed as disease.

A recent review of the literature (8) listed the independently replicated risk factors for relapse among patients who had sought treatment for unipolar depression. There were three such factors: a history of recurrence (6, 8), young age (7, 10, 11), and a diagnosis of secondary depression (7, 12). Thus, the agreement between the clinically based literature and the present follow-up of a nonclinical study group is striking, supports the validity of both the design and the results of our study, and suggests that these conclusions can be broadly generalized. Youth and nonaffective disorder deserve special emphasis because these factors raise the risk for first onset of depression as well (1).

Clinical implications follow from this broad generalizability. Patients often find comfort in a description of the natural history of their disorder, since this reduces, at least somewhat, uncertainties regarding the future. Clinicians may also wish to be more cautious about discontinuing antidepressant prophylaxis when these risk factors are prominent.

There are several broad, unanswered but research-

able questions. How do nonaffective illnesses promote the onset and recurrence of major depressive disorder? Why does primary depression become less likely with increasing age? The answers are obviously relevant to the fundamental mechanisms of affective disorder. Whatever the answers, though, these findings can aid the clinician in predicting long-term outcome. They should also be considered in the evaluation of treatments studied for their prophylactic efficacy.

ACKNOWLEDGMENTS

The National Institute of Mental Health Collaborative Program on the Psychobiology of Depression—Clinical Studies was conducted with the participation of the following investigators: M.B. Keller, M.D., Chairperson (Boston/Providence); G.L. Klerman, M.D., Co-Chairperson (New York); J. Maser, Ph.D. (Washington, D.C.); P.W. Lavori, Ph.D., and M.T. Shea, Ph.D. (Boston/Providence); J.A. Fawcett, M.D., W.A. Scheftner, M.D., and M. Young, Ph.D. (Chicago); W. Coryell, M.D., and J. Haley, B.A. (Iowa City); J. Endicott, Ph.D., and J.E. Loth, M.S.W. (New York); J. Rice, Ph.D., and T. Reich, M.D. (St. Louis). Other contributors include N.C. Andreasen, M.D., P.J. Clayton, M.D., J. Croughan, M.D., R.M.A. Hirschfeld, M.D., M.M. Katz, Ph.D., E. Robins, M.D., R.W. Shapiro, M.D., R.L. Spitzer, M.D., and G. Winokur, M.D.

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Outcome of Schizoaffective Disorder at Two Long-Term Follow-Ups: Comparisons With Outcome of Schizophrenia and Affective Disorders

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Objective: This research assessed whether the outcome of schizoaffective disorder is more similar to that of schizophrenia or that of affective disorders. **Method:** The authors conducted a prospective follow-up study of 101 schizoaffective, schizophrenic, bipolar manic, and depressed patients assessed at three times: during hospitalization and 2 and 4–5 years later. The follow-up test battery involved detailed assessment of social functioning, work performance, symptoms, posthospital treatment, and rehospitalization. **Results:** Outcome for schizoaffective patients 4–5 years after hospitalization differed significantly from that for patients with unipolar depression. However, the differences between schizoaffective and bipolar manic patients were more equivocal. Unlike the patients with bipolar disorder, only a limited number of patients with schizoaffective disorder showed complete recovery in all areas throughout the year preceding the 2-year follow-up and the year preceding the 4- to 5-year follow-up. The differences in outcome between schizoaffective and schizophrenic patients were also mixed. These two groups showed some similarities in outcome, but there were fewer schizoaffective than schizophrenic patients with uniformly poor outcome in all areas. **Conclusions:** Overall, schizoaffective patients showed some similarities to both schizophrenic and bipolar manic patients. Schizoaffective patients had somewhat better overall posthospital functioning than patients with schizophrenia, somewhat poorer functioning than bipolar manic patients, and significantly poorer functioning than patients with unipolar depression. The data suggest that when mood-incongruent, schizophrenic-like psychotic symptoms are present in the acute phase, they predict considerable difficulty in outcome, even when affective syndromes are also present, as in schizoaffective disorder. It is likely that schizoaffective disorder is not just a simple variety of affective disorder.

(Am J Psychiatry 1991; 148:1359–1365)

Ever since 1933 when Kasanin first coined the term “schizoaffective” to describe patients who presented with simultaneous schizophrenic and affective syndromes, there has been a debate about whether schizoaffective disorder is more accurately considered as a form of schizophrenia (1), a form of affective disorder (2), a separate entity distinct from both (3), or

part of a continuum that includes both. The issue of how to conceptualize schizoaffective disorder is central to theoretical considerations of diagnosis and nosology and to considerations of treatment. The present study addressed these issues by providing data on the course of illness in schizoaffective disorder and on the relation of schizoaffective disorder to schizophrenia and major affective disorders.

There are various ways to categorize patients who have both full affective syndromes and full schizophrenic syndromes, and various cutoff criteria have been applied. One diagnostic scheme is the Research Diagnostic Criteria (RDC) (4), which is widely used in a number of major research programs. At present, solid evidence about which schemes are best (e.g., DSM-III-R, the RDC, or other schemes) is still missing from the literature. We studied patients with simultaneous psychotic and affective syndromes, diagnosed according to

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Supported in part by NIMH grant MH-26341 and by a research grant from the John D. and Catherine T. MacArthur Foundation.

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the RDC as having schizoaffective disorder, with the goal of providing additional data on their posthospital functioning at several successive follow-up times.

One of the important criteria for validating a diagnostic entity such as schizoaffective disorder is the long-term course of illness, because it permits assessment of whether the diagnosis includes patients whose clinical courses differ from those of patients with other types of disorders (e.g., whether outcome for patients with schizoaffective disorder is more similar to that for patients with schizophrenia or affective disorders). If the more historical view reflected by *DSM-II*—that schizoaffective disorder is a type of schizophrenia—is accurate, then schizoaffective patients would be expected to show a course of illness which is more similar to schizophrenia than to affective disorders. Research on this question has produced mixed results (3, 5, 6).

Another related issue that has received much recent research attention is the relative prognostic importance of affective and of schizophrenic symptoms. A number of studies have reported that prominent affective symptoms are related to good outcome (7). However, other studies have reported that schizoaffective patients (or patients with atypical schizophrenia) have significantly poorer global outcomes than do patients with affective disorders (8–13) and that the outcome of schizoaffective disorder may not be distinguishable from that of schizophrenia (13, 14). These findings could suggest that mood-incongruent psychotic symptoms are associated with poor outcome, regardless of whether affective symptoms also are present (9). A number of other studies have reported that the outcome of schizoaffective disorder is more favorable than the outcome of schizophrenia (8, 12, 15–17).

These issues concerning the course and outcome of schizoaffective disorder have not been examined before with schizoaffective patients studied prospectively three times: at index hospitalization and then during two successive follow-up periods. Our research was designed to study these issues and to provide information on the following questions.

1. What is the course of schizoaffective disorder when patients are studied during hospitalization and then prospectively at two successive follow-ups?
2. Is the course of illness of schizoaffective patients more similar to that of patients with affective disorders or to that of schizophrenic patients?
3. Are mood-incongruent schizophrenic-like psychotic symptoms important in predicting outcome?

METHOD

The subjects in the current study were 101 psychiatric patients who were studied first when they were hospitalized and were then followed up prospectively 2 years after hospitalization and again 4–5 years after hospital discharge. Seventy-four patients (73%) from this group were assessed as part of the Chicago Follow-Up Study, a longitudinal research program based at Michael

Reese Hospital and the Illinois State Psychiatric Institute, for studying thought disorder, psychosis, and posthospital functioning (9, 18–22). Fifty-three of these Chicago Follow-Up Study patients were originally hospitalized at Michael Reese Hospital and 21 were hospitalized at the Illinois State Psychiatric Institute. The remaining 27 patients in our study group were hospitalized at the Illinois State Psychiatric Institute as part of a Mental Health Clinical Research Center program (23) and then followed up by us, using the same research instruments for data collection that were used with the other patients. Slightly more than 80% of the original group who were assessed as inpatients were followed up twice.

Overall, the study group included 41 schizoaffective patients, 20 schizophrenic patients, 20 bipolar manic patients, and 20 patients with major depressive disorder. All of the schizoaffective and schizophrenic patients were psychotic at index hospitalization, as were 82% of the bipolar manic patients (i.e., 14 of the 17 bipolar patients for whom these data were available). Sixteen (80%) of the 20 depressed patients were not psychotic during the index hospitalization. The four depressed patients who were initially psychotic did not differ on the outcome measures from the depressed patients who were not initially psychotic, although differences in outcome have emerged in previous analyses of larger samples of psychotic depressed patients (24). All but two of the depressed patients had unipolar depression, and those two patients had never had a full manic syndrome (i.e., they were diagnosed as having bipolar II disorder). All patients from the Chicago Follow-Up Study were diagnosed according to the RDC at index hospitalization on the basis of information obtained from the Schedule for Affective Disorders and Schizophrenia (SADS) (25), from an additional semistructured, tape-recorded clinical interview (18), and from extensive inpatient observations. The Mental Health Clinical Research Center patients were given diagnoses according to the RDC on the basis of information derived from the SADS and the Present State Examination (PSE) (26).

At index hospitalization, the patients had a mean \pm SD age of 24.5 ± 5.0 years. They had completed a mean \pm SD of 13.78 ± 2.63 years of school. Forty-four percent were female, 67% were white, and 33% were black. Illinois State Psychiatric Institute patients tended to come from lower- or lower-middle-class backgrounds, while Michael Reese Hospital patients tended to come from middle- to upper-middle-class backgrounds. The patients thus represented a relatively young group from a broad range of social classes. Analyses showed no major differences in overall outcome between the patients from the higher social classes and those from the lower, although there was a nonsignificant tendency toward better posthospital work functioning for patients from the higher social classes. There were no significant differences among the four diagnostic groups in age ($F=0.44$, $df=3$, 97, $p>0.50$) or education ($F=0.94$, $df=3$, 97, $p>0.40$). A larger percentage of schizophrenic patients

TABLE 1. Overall Outcome for Patients With Schizoaffective Disorders and Patients in Other Major Diagnostic Groups at Two Follow-Up Times

Diagnostic Group	First Follow-Up (2 years after hospitalization)				Second Follow-Up (4–5 years after hospital discharge)			
	Overall Score on Strauss- Carpenter Scale ^a		Patients With Very Poor Outcome ^b		Overall Score on Strauss- Carpenter Scale ^a		Patients With Very Poor Outcome ^b	
	Mean	SD	N	%	Mean	SD	N	%
Schizoaffective disorder (N=41)	9.68	4.0	17/40	43	9.73	3.3	17/40	43
Schizophrenia (N=20)	9.40	4.7	11/20	55	8.60	3.9	11/20	55
Bipolar manic disorder (N=20)	10.40	4.0	7/20	35	10.08	3.5	4/14	29
Major depressive disorder (N=20)	10.60	3.4	2/20	10	10.20	3.5	2/15	13

^aOn this 16-point scale, higher scores reflect better functioning.

^bLKP Scale score of 7 or higher.

than of affective disorder or schizoaffective patients were male, which is consistent with typical sex distributions across diagnostic groups.

The median number of hospitalizations before the index hospitalization for the total group of patients was 1.3, and 62% of the patients had experienced only one or no hospitalization before the index hospitalization. For the group of relatively young schizoaffective patients, the majority of whom did not have a large number of previous hospitalizations, there was no significant association between the number of previous hospitalizations and overall outcome.

The follow-up evaluations included a structured interview that was designed to assess various areas of functioning, a series of personality tests, several questionnaires, and the SADS. The follow-up test battery involved detailed assessment of 1) social functioning, work performance, and family adjustment, 2) the patients' subjective evaluations of their own mental health, 3) psychotic, anxiety, and affective symptoms, 4) key personality features, 5) cognitive functioning and thought disorder, 6) posthospital psychotherapy and medication, and 7) incidence of rehospitalization during the last year before each of the two follow-up assessments. The follow-ups were conducted by trained investigators who were not informed of the patients' diagnostic status.

We used two major instruments to evaluate patients' illness with respect to specific areas of functioning and overall adjustment. The first outcome index, developed by Strauss and Carpenter (27), takes into account four important areas of functioning: symptoms, rehospitalization, social functioning, and employment. The summation of these four individual subscale scores also provides a composite rating of overall adjustment at follow-up.

The second measure of overall outcome, the "LKP Scale" developed by Levenstein et al. (28), is based on work and social functioning, life disruption, self-support, symptoms, relapse, rehospitalization, and suicide. The LKP Scale can be used to categorize patients according to whether they showed uniformly poor outcomes in all areas or almost all areas of functioning (e.g., both psychosis and poor psychosocial function-

ing). Both the Strauss-Carpenter Scale and the LKP Scale have been shown to have good reliability and have been used previously in a number of major outcome studies (9, 21, 22, 24, 27, 28).

RESULTS

The outcome data were subjected to two-way mixed design analyses of variance (ANOVAs) with one repeated measure factor. In these ANOVAs, the two main effects were diagnosis and time of assessment or phase of disorder (the repeated measure factor).

Overall Adjustment

Table 1 shows the level of overall functioning for each diagnostic group at both follow-up assessments according to the Strauss-Carpenter Scale and the LKP Scale. Results were similar for the two measures.

1. In the ANOVA on overall functioning, the main effect for diagnosis was significant ($F=4.38$, $df=3$, 97, $p<0.006$). This significant main effect for diagnosis occurred because the schizoaffective, schizophrenic, and bipolar patients showed poorer posthospital functioning than did the depressed patients. The main effect for time of assessment was not significant ($F=1.57$, $df=1$, 3, n.s.), indicating that there were no significant changes in overall functioning over time between the 2-year and the 4- to 5-year follow-ups. There was no significant interaction effect.

2. At the first follow-up assessment, the schizoaffective group was functioning slightly better than the schizophrenic group and slightly worse than the bipolar manic group. The depressed patients were functioning at a significantly higher level than the relatively inadequate level of the schizoaffective patients ($p<0.05$, as shown by Newman-Keuls tests for post hoc comparisons).

3. At the second follow-up assessment, the pattern of differences among diagnostic groups in overall functioning was similar. The schizoaffective, schizophrenic, and bipolar manic patients again showed the poorest overall functioning. As at the first follow-up assess-

ment, the depressed patients showed significantly better overall functioning than did the other three groups ($p < 0.05$).

4. To determine whether the major differences among diagnostic groups (i.e., the differences between the schizoaffective and depressed patients) held for each of the two research programs, separate two-way repeated measures ANOVAs were conducted for each institution. The ANOVAs within each research program showed significantly poorer functioning for schizoaffective patients than for depressed patients. At each of the settings, there was no difference across follow-up period, nor was there a significant interaction. Similarly, to determine whether the differences between the schizoaffective and depressed patients held for women alone and for men alone, we analyzed the data separately for each sex, using separate two-way repeated measures ANOVAs. The results indicated significant differences among diagnostic groups for the women ($F=7.08$, $df=1, 28$, $p < 0.05$) and nearly significant differences for the men ($F=3.73$, $df=2, 39$, $p < 0.10$). For each sex, there was no difference for time period and no significant interaction.

5. The slightly better functioning of the schizoaffective patients than the schizophrenic patients at both follow-up times was due in part to the smaller proportion of schizoaffective patients than of schizophrenic patients who showed uniformly poor outcome in the major areas of functioning. Thus, we conducted separate statistical analyses of the number of patients in each diagnostic group who showed uniformly poor outcome, using the criteria of the LKP Scale for poor outcome (i.e., severe symptoms and very poor psychosocial adjustment). The results indicated significant differences among diagnostic groups at both the first follow-up ($\chi^2=9.45$, $df=3$, $p=0.02$) and the second follow-up ($\chi^2=7.73$, $df=3$, $p=0.05$). At the first follow-up, 43% of the schizoaffective patients showed uniformly poor outcome, in contrast to 55% of the schizophrenic patients. At the second follow-up also, 43% of the schizoaffective patients showed uniformly poor outcome, in contrast to 55% of the schizophrenic patients, although it was not the exact same group of patients showing poor outcome at each follow-up.

6. The results of the statistical analyses indicated that although there was a greater proportion of schizophrenic than of schizoaffective patients with very poor outcomes, these two patient groups did not differ significantly from each other in overall functioning. The schizoaffective patients showed slightly poorer overall outcome than the bipolar manic patients, but these differences also were not even close to being significant.

While the schizoaffective patient group tended to show an outcome pattern which differed from the patterns of the schizophrenic patients and the bipolar manic patients, at both follow-ups they did not differ significantly from these groups in overall functioning. The lack of a significant difference between the schizoaffective and schizophrenic patients was due, in part, to the fact that although very few schizophrenic patients

showed complete recovery in every major area, only a limited number of schizoaffective patients showed complete recovery in all areas throughout the year preceding the 2-year follow-up and the year preceding the 4- to 5-year follow-up.

The complete pattern of data on functioning and adjustment tended to show the schizophrenic patients as having the poorest overall outcome, but the great majority of the schizoaffective patients also tended to show major problems in at least some areas of adjustment at both follow-ups. The bipolar manic patients showed somewhat better functioning than the schizoaffective patients, and the depressed patients showed significantly better functioning in a number of areas than the other three groups. If outcome for major diagnostic groups is used as one criterion to provide clues to the similarities among diagnostic groups, as has been suggested by Procci (3), the data could suggest that schizoaffective disorder is a diagnostic entity distinct from major depressive disorder in terms of poorer overall adjustment.

Schizoaffective Subtypes: Overall Adjustment

Contrary to some hypotheses (8), there were no significant differences in overall outcome between patients with schizoaffective disorder, manic type, and those with schizoaffective disorder, depressive type, at the first follow-up ($t=0.05$, $df=39$, $p > 0.15$) or at the second ($t=0.37$, $df=39$, $p > 0.15$). However, 33 of the 41 schizoaffective patients who entered this study had the depressive type of the disorder. Thus, hypotheses in this area still need to be evaluated with a larger sample of patients with schizoaffective disorder, manic type.

Similarly, there were no significant differences in overall outcome between the schizoaffective, mainly affective, and the schizoaffective, mainly schizophrenic, patients, although there was a trend for poorer outcome for the schizoaffective, mainly schizophrenic, patients at the second follow-up ($t=1.59$, $df=33$, $p=0.12$). Since this issue has been of some theoretical interest, further exploration would seem worthwhile.

Medications

A separate analysis was conducted to study potential differences in outcome between patients taking psychotropic medications and those not taking such medications at follow-up. However, caution is needed in interpreting the medication data, because patients were not assigned to treatment groups at random. In many cases, patients' poorer clinical conditions may have been the reason they were being treated with medication.

A detailed analysis was conducted for the group of schizoaffective patients at both follow-ups. The analysis compared 1) schizoaffective patients taking no medication ($N=14$ at the first follow-up), 2) those taking lithium either alone or in combination with any other medications ($N=6$ at the first follow-up), and 3) those

TABLE 2. Rehospitalization of Patients With Schizoaffective Disorders and Patients in Other Major Diagnostic Groups at Two Follow-Up Times

Diagnostic Group	First Follow-Up (2 years after hospitalization)				Second Follow-Up (4–5 years after hospital discharge)			
	Rehospitalization Score on Strauss- Carpenter Scale ^a		Patients Rehospitalized		Rehospitalization Score on Strauss- Carpenter Scale ^a		Patients Rehospitalized	
	Mean	SD	N	%	Mean	SD	N	%
Schizoaffective disorder (N=41)	3.24	1.2	16	39	3.46	0.9	15	37
Schizophrenia (N=20)	3.10	0.8	9	45	3.55	0.5	8	40
Bipolar manic disorder (N=20)	3.45	0.8	9	45	3.60	0.6	7	35
Major depressive disorder (N=20)	3.65	0.7	5	25	3.75	0.6	4	20

^aOn this 5-point subscale, higher scores reflect better functioning.

taking neuroleptics alone or in combination with medications other than lithium (N=21 at the first follow-up). There were no significant differences in outcome among the schizoaffective patients under the three treatment conditions at either the first follow-up ($F=2.88$, $df=2, 38$, $p=0.07$) or the second ($F=2.10$, $df=2, 38$, $p=0.14$). There was a nonsignificant tendency at both follow-ups for schizoaffective patients who were treated with neuroleptics to show more difficulty in functioning than those not taking neuroleptics. In general, both the schizoaffective patients who were treated with lithium and those not so treated tended to experience at least some difficulty in functioning, with no significant difference between the two treatment groups.

Medication data were also analyzed for the other diagnostic groups at the second follow-up, and similar results were obtained. Medicated schizophrenic patients showed more pathology than did unmedicated schizophrenic patients ($t=2.58$, $df=18$, $p<0.02$). There were no significant differences in outcome for the bipolar manic patients ($t=1.12$, $df=18$, $p>0.20$).

Psychosis and Rehospitalization

One key issue in considering how schizoaffective disorder should be classified is whether it shows the level of psychotic symptoms found in schizophrenia or affective disorders. Thirty-four percent (N=14) of the schizoaffective patients showed clear psychosis at the first follow-up, and another 27% (N=11) showed equivocal signs of psychosis. There was little difference in the level of psychosis between the schizoaffective and schizophrenic patients at the first follow-up.

At the second follow-up, 32% (N=13) of the schizoaffective patients showed clear psychosis, and another 12% (N=5) showed equivocal signs. At the second follow-up, the schizoaffective patients tended to show less psychosis than the schizophrenic patients, although the difference was not significant. At the 2-year and the 4- to 5-year follow-ups, both the schizoaffective and the schizophrenic patients showed significantly more psychosis than the depressed patients. The schizoaffective and schizophrenic patients also tended to show more psychosis than the bipolar manic patients at each follow-up, but the differences were not significant.

The schizoaffective patients showed a slight but non-significant improvement, in terms of less psychosis, as they moved from the first to the second follow-up. The schizophrenic patients did not show such an improvement from the first to the second follow-up.

Table 2 shows the rehospitalization data for each diagnostic group at both follow-ups. The data for these patients, who were assessed early in the course of their disorders, indicate that all diagnostic groups at both follow-ups had been rehospitalized an average of less than 3 months in the last year (indicated by a score of 3). In the ANOVA on the Strauss-Carpenter rehospitization subscale scores, the main effect for time period was not significant ($F=3.10$, $df=1, 3$, $p=0.08$), although all four diagnostic groups spent less time in the hospital during the second follow-up period than the first. There were no significant differences in rehospitization among the diagnostic groups at the two follow-ups ($F=0.92$, $df=3, 97$, *n.s.*). However, there was a strong trend at both follow-ups toward fewer rehospitalizations for the depressed patients than for the other three groups.

Social and Work Functioning

The patients' mean scores on the Strauss-Carpenter social functioning subscale fell between 2.6 and 3.6. On this scale, a score of 2 indicates that patients socialized with friends approximately once per month, a score of 3 indicates two to three times per month, and a score of 4 indicates at least once per week. Sixty-three percent of the total group socialized with friends either two to three times per month or more frequently, and 63% (N=26) of the schizoaffective patients also showed this level of social contact.

The two-way ANOVA for scores on this subscale indicated no significant differences among diagnostic groups in social functioning, although there was a trend for the depressed patients to socialize more frequently than the other groups. Thus, at the first follow-up, the schizoaffective patients' mean±SD score was 2.76 ± 1.56 , and the depressed patients' score was 3.55 ± 0.94 ($t=2.09$, $df=59$, $p=0.04$). At the second follow-up, there was also a trend in the same direction ($t=1.68$, $df=59$, $p<0.10$). There was a significant main effect for time of

assessment, which indicated that all diagnostic groups experienced some decline in social functioning over time. At the first follow-up the total group's mean score was 3.04 ± 1.41 ; at the second follow-up it was 2.76 ± 1.38 ($F=4.82$, $df=3$, 97 , $p<0.03$).

The patients' mean employment scores were between 1.5 and 3.6. On this subscale, a score of 2 indicates that patients were employed part-time or full-time for about half of the past year, and a score of 3 indicates employment for more than half a year, but less than continuously.

The main effect for diagnosis in the two-way ANOVA on the Strauss-Carpenter employment subscale scores was significant ($F=3.84$, $df=3$, 97 , $p=0.01$), with the schizoaffective, schizophrenic, and bipolar manic patients showing poorer posthospital work adjustment than the depressed patients. The main effect for time of assessment was not significant, despite a minor trend for patients to show poorer work functioning over time ($F=2.85$, $df=1$, 97 , $p>0.14$). There was no significant interaction effect.

DISCUSSION

Overall Outcome: Schizoaffective Disorder Versus Schizophrenia and Affective Disorders

The major issue on which the current research was centered is whether the clinical course of schizoaffective disorder is more similar to that of schizophrenia or affective disorders.

Regarding the first alternative, the results were mixed. Schizoaffective patients at both follow-ups showed some similarities in outcome to schizophrenic patients on the indexes we used, although there was a nonsignificant tendency on all of the outcome measures for the schizoaffective patients to show better functioning than the schizophrenic patients. This was particularly noticeable in terms of the smaller percentage of schizoaffective patients than schizophrenic patients with uniformly poor outcome in almost all major areas. These results were found at both follow-ups, with slightly over 40% of the schizoaffective patients showing uniformly poor outcome, as opposed to a much larger percentage of the schizophrenic patients.

While there was a smaller proportion of schizoaffective than of schizophrenic patients with uniformly poor outcomes, the schizoaffective patients were generally found to be experiencing considerable difficulties at the first follow-up 2 years after hospital discharge, and the data from the second follow-up indicated that their functioning improved only slightly from the 2-year follow-up to the 4- to 5-year follow-up. These results bear directly on recent theoretical controversies in the literature about how schizoaffective disorder should be viewed. They suggest many similarities with schizophrenia, although there are some clear differences—especially, a tendency for fewer schizoaffective patients to show uniformly poor outcome in all areas.

For the second major alternative—that outcome of

schizoaffective disorder is similar to that of bipolar and unipolar affective disorders—the data are clear on potential differences between schizoaffective patients and patients with unipolar depression. At both follow-up assessments, the schizoaffective patients' overall functioning and work performance were significantly less favorable than were those of the unipolar depressed patients.

While outcome for the schizoaffective patients 4–5 years after hospitalization differed significantly from that of the unipolar depressed patients, there were more mixed or equivocal results on potential differences between the schizoaffective patients and the patients with bipolar disorder. These differences were much smaller and not statistically significant. A number of the bipolar manic patients showed difficulties in functioning. More of the schizoaffective patients showed difficulties, and more showed uniformly poor outcomes, but the lack of significant differences between the patients with schizoaffective and bipolar manic disorders does not permit a definitive answer concerning potential differences between these two diagnostic groups. At present the case for differentiating these two groups according to outcome is not proven, although there are clear suggestions of differences.

Thus, the results indicate clear differences in outcome between patients with schizoaffective disorder and patients with unipolar depression and suggest possible differences between schizoaffective and bipolar manic patients, but in the latter comparison the differences are not definitive. In general, there were no significant differences at two follow-up times between schizoaffective patients and the other two severely disordered groups (e.g., the schizophrenic and the bipolar patients). However, there were consistent differences in the directions one would predict (i.e., the overall outcome for the schizoaffective patients was intermediate between the outcomes for the other two groups).

Vulnerability and the Prognostic Significance of Mood-Incongruent Psychotic Symptoms

Pope and Lipinski (15), in discussing schizophrenic patients, have proposed that psychotic symptoms are not effective prognostic indicators, while affective symptoms are prognostic of good outcome. The results from the current research, as well as data we have previously reported (9, 20), could be interpreted as suggesting that the presence of mood-incongruent, schizophrenic-like psychotic symptoms at the acute phase of hospitalization is important in marking potential vulnerability to poor outcome, both in schizoaffective patients who also have major affective syndromes and in schizophrenic patients who do not have major affective syndromes during hospitalization.

Thus, our data do not support the views of Pope and Lipinski (15), since the great majority of our patients with mood-incongruent schizophrenic-like psychotic symptoms showed at least some difficulties on measures of outcome, and a number had poor outcomes in almost all areas during the next 4 years, regardless of

whether they were schizoaffective or schizophrenic patients. In addition, some of the bipolar manic patients had poor outcomes despite the prevalence of their affective symptoms during hospitalization (21). Our data from two successive follow-ups suggest that mood-incongruent, schizophrenic-like psychotic symptoms in the acute phase are predictive of considerable difficulty in outcome for many patients, even when affective syndromes also are present, as in schizoaffective disorders.

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Psychiatric Consultation to a State Board of Medical Examiners

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This article describes the evolution of psychiatric consultation to the Oregon Board of Medical Examiners. The board is charged with the licensing and regulation of physicians in the state of Oregon in order to protect the public and uphold the standards of the medical profession. Psychiatric consultation has focused on the board's investigations of physicians with mental illness and/or substance abuse and physicians who inappropriately prescribe psychoactive drugs or sexually abuse patients. Each of these physician groups is described, and remedial programs for each group are discussed. The authors conclude that psychiatric consultation to medical boards is a feasible and productive activity that can make a positive contribution to the lives of a large number of physicians and patients.

(Am J Psychiatry 1991; 148:1366-1370)

The regulation of medicine has become a significant factor in the lives of physicians, who face increasing problems with credentialing at all levels of medical practice (1). As a result of these changes, the roles and responsibilities of state medical boards of licensure and discipline have increased dramatically. These bodies serve as lightning rods for legislators, insurers, consumers, hospitals, and medical societies, many with conflicting agendas, all attempting to shape the practice of medicine (2). A significant issue for each medical board is how to balance concerns about the protection of the general public with concerns about the rights and privileges of physicians. This is a particularly difficult balance to strike when there is a question of physician impairment.

This article describes the evolution of psychiatric consultation to the Oregon Board of Medical Examiners as it meets its statutory obligations to the citizens and to the physicians of the state of Oregon. The Oregon board has been one of the most active state medical boards; it has ranked sixth nationwide in the number of disciplinary actions taken per 1,000 physicians (3). At

the same time, it has also maintained a major focus on rehabilitation of troubled physicians.

THE OREGON BOARD OF MEDICAL EXAMINERS: PURPOSE, MEMBERSHIP, AND PROCESS

Members of the board, nine physicians and two lay members, are appointed by the governor for 4-year terms. The purpose of the board is defined in statute:

Recognizing that to practice medicine is not a natural right, but is a privilege granted by legislative authority, it is necessary in the interests of the health, safety and welfare of the people of this state to provide for the granting of that privilege and the regulation of its use, to the end that the public is protected from the practice of medicine by unauthorized or unqualified persons and from unprofessional conduct by persons licensed to practice under this chapter. (4)

The statutes list 27 potential grounds for suspending, revoking, or refusing to grant a medical license (5).

To carry out its responsibilities, the board meets on a quarterly basis. Much of the work in preparation for these meetings is accomplished through two key committees. The Administrative Affairs Committee meets prior to each quarterly meeting and reviews problematic applications for licensure. The Investigative Committee meets monthly and reviews complaints made against licensed physicians. If a complaint is deemed to be a possible statutory violation, the physician is scheduled for an interview before the Investigative Committee. If the committee determines that a violation may have taken place, the committee refers the situation to the quarterly board meeting for final decision.

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Supported in part by the Oregon Foundation for Medical Excellence.

The authors thank Donald Dobson, M.D., Medical Director of the Oregon Board of Medical Examiners, for his help with this project.

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The full board has several options. It can terminate the case or initiate some form of disciplinary action. The board may offer to enter into a voluntary agreement with the physician based on a plan for dealing with the defined problem. The board can also place the physician on formal probation or initiate procedures that could result in a revocation of the physician's license. Probation or a voluntary limitation allows the board to monitor physicians for a prescribed period of time.

PSYCHIATRIC CONSULTATION TO THE BOARD

Psychiatric consultation began in 1978 following several suicides of physicians on probation (6). The initial consultant was chosen by the board because of his interest in substance abuse and suicide prevention, his academic affiliation, and his interest in research. The consultant focused on helping the board develop evaluation procedures for individual cases, understand psychiatric data, develop treatment resources, and initiate research on the effectiveness of rehabilitation (7).

Over the years the role has expanded. The consultant now attends all meetings of the Administrative Affairs and Investigative Committees and significant portions of the quarterly meetings of the full board. At these meetings the consultant participates in discussion of the psychiatric issues involved in individual cases but not in the formal voting process that determines the disposition of the cases. The consultant adds to the board's deliberations by maintaining a long-term perspective on individual cases, a familiarity with the research literature, and a dispassionate involvement with the board's group process.

THE FOCUS OF PSYCHIATRIC CONSULTATION

The psychiatric consultation initially focused on physicians impaired by mental illness and/or substance abuse. In recent years the focus has expanded to include inappropriate prescribing of psychoactive drugs and sexual abuse of patients. Each is briefly described in this article. To put these areas into some perspective, table 1 shows the reasons for investigation in the cases evaluated by the Investigative Committee from 1981 to 1988. Inappropriate prescribing accounted for half of the investigations, followed by substance abuse and mental illness. Sexual abuse is an area where we are just beginning systematic investigation. The 43 cases listed in table 1 for inappropriate behavior include investigations involving sexual abuse but also include other forms of inappropriate behavior. The discussion of sexual abuse in this article covers 11 documented cases from 1985 to 1990.

Physicians Impaired by Mental Illness and/or Substance Abuse

Major efforts toward the rehabilitation of physicians impaired by mental illness and/or substance abuse date

TABLE 1. Reasons for Investigation in 377 Cases of Physician Impairment in Which Psychiatric Consultation Was Used (1981-1988)

Reason	N	%
Inappropriate prescribing	189	50
Substance abuse	39	10
Mental illness	16	4
Inappropriate behavior	43	11
Other (primarily inappropriateness of medical treatment)	90	24

to the early 1970s, when the American Medical Association (AMA) focused the attention of the medical community on the problems of impaired physicians (8).

Substance abuse. Following the AMA's initiative, substantial progress has been made in the development of collaboration between medical boards and treatment programs for substance-abusing physicians. Reports from Georgia (9), California (10), and Oregon (11, 12) all indicate success in treating physicians for substance abuse. The treatment approach focuses on early identification of these physicians and active intervention. Intervention is frequently followed by a period of residential treatment in a facility specializing in the care of substance-abusing physicians. After inpatient treatment the physician is typically placed on probation, is allowed to return to work, and is enrolled in a monitored treatment program emphasizing group therapy, random urine drug screening, and involvement in 12-step programs (13).

In 1987 Shore (12) reported an 8-year experience with 63 physicians on probation with the board. He demonstrated an overall improvement rate of 75% for physicians on probation. He also reported that monitored treatment led to better outcome than treatment without accompanying urine drug screening.

The average length of the monitored program in uncomplicated cases is now approximately 5 years, although the board may keep a physician in a monitored program for a 10-year period. Cases may be complicated by either a major relapse or an additional diagnosis of a major mental illness or personality disorder.

Recently, the board initiated a semiautonomous diversion program funded by an increase in medical license fees. This program, similar in design to a program developed in Colorado (14), emphasizes early identification of substance-abusing physicians and referral of these physicians to voluntary treatment. The diversion program operates independently of the board and reports physicians to the board only after the failure of voluntary treatment.

Mental illness. The board sees relatively few physicians with major mental illness. Referred physicians most commonly fall into two diagnostic categories, organic mental disorders and bipolar disorder.

Physicians with organic mental disorders usually come before the board following a known traumatic brain injury or stroke. Some are referred to the board because of suspected problems with medical competency. These are usually older physicians who upon

evaluation are found to demonstrate evidence of organic mental disorder. The most common action in these instances is a voluntary agreement between the physician and the board for either suspension of the physician's medical license or retirement.

Physicians with bipolar disorder often come to the attention of the board during licensure deliberations or, for those already licensed, during a hypomanic or manic episode, most often associated with hospitalization. Since 1981 there have been six physicians placed on formal probation for bipolar illness, four with associated substance abuse. The probation involves regular monitoring by a psychiatrist approved by the board, who reports to the board on a quarterly basis. In addition, the physician is regularly seen by the board. Three other physicians have entered into a voluntary agreement with the board for psychiatric monitoring of their bipolar illness, with provision for periodic reports to the board regarding their mental condition.

The board sees few physicians suffering from other major mental illnesses. In the 12 years of psychiatric consultation, only one physician has been considered to suffer from schizophrenia. There have been several referrals of individuals with late-onset paranoid disorders. It is rare for physicians with depressive disorders to come to the attention of the board except during licensing, when past psychiatric treatment is asked about. Occasionally, a depressed physician will come to the attention of the board following a major suicide attempt associated with hospitalization. Presentation to the board because of anxiety disorders is also rare except when these are associated with self-medication and/or substance abuse.

Over the last 5 years the board has not seen a physician suffering from a paraphilia as defined by *DSM-III-R*. In cases involving the question of inappropriate sexual advances to minors, evaluations to rule out pedophilia, including the measurement of sexual arousal patterns, are undertaken. Three physicians were evaluated for inappropriate contact with minors. None suffered from pedophilia, but each demonstrated problems that affected the practice of medicine. Each was placed on probation and enrolled in a therapy program.

Physicians Who Prescribe Psychoactive Drugs Inappropriately

In 1985 the psychiatric consultation was extended to cases of suspected inappropriate prescribing of psychoactive drugs. This is an important area of interest for medical boards because of professional and public concerns about narcotic drug prescriptions, primarily in the management of chronic pain patients (15). In Oregon one of the grounds for potential refusal to grant a license or for revoking a license is "prescribing controlled substances without a legitimate medical purpose and without following accepted procedures for examination of patients and record keeping" (16).

In 1986 we initiated a research project designed to examine characteristics of physicians charged with in-

appropriate prescribing and how these cases were handled by the board (17, 18). From 1981 to 1986, 51% (N=154) of the 300 complaints that reached the stage of informal interview with the Investigative Committee were for alleged inappropriate prescribing. Sixty-five percent (N=85) of the physicians were primary care physicians. Fifty-five percent (N=73) of the patients were chronic pain patients, and 24% (N=32) were drug-seeking patients.

Fifty-eight percent (N=75) of the cases referred for inappropriate prescription writing were terminated at the Investigative Committee level, and 42% (N=55) went on to a hearing before the full board. Of the group referred to the board, 64% (N=35) agreed to a voluntary limitation of their prescribing privileges for scheduled drugs.

This research project identified several areas of concern. Many physicians had significant gaps in their knowledge about the use of narcotics for treating chronic pain. Physicians had difficulty in recognizing substance-abusing patients, and when such patients were known, they had difficulty in managing them appropriately. We identified, in many of these physicians, psychological factors that we believed contributed heavily to the inappropriate prescribing, including a strong orientation to immediate symptom relief, great difficulty in setting limits with patients, and difficulty in handling negative affects, both their own and those of the patients. In many cases there was also an element of grandiosity which led the physician to believe that he or she could help the patient after other doctors had failed.

This research project contributed to the development of expanded educational activities for the general medical community that were focused on the rational management of chronic pain patients. For the physicians identified by the board as needing additional attention, a remedial workshop was established that focused on chronic pain, the recognition of drug-seeking and drug-abusing patients, limit setting, and other problems associated with inappropriate prescribing. The board also required some physicians to enter a triplicate-prescription program. In the more extreme cases, or in those in which the physician continues to have problems even after educational approaches have been attempted, the board can institute a limitation on the physician's ability to prescribe scheduled drugs.

Physicians With Problems of Sexual Abuse

During the last decade this topic has received increased national attention from the professional (19) and legal (20) communities as well as from the national media. Over the past 5 years, the board has begun to develop a systematic approach to this problem. Sexual abuse is defined as occurring within the physician-patient relationship and includes inappropriate touching, inappropriate physical examination, and/or sexual intercourse.

From 1985 to the middle of 1990, 11 physicians came before the board following accusations of sexual in-

volvement with patients. This group included four psychiatrists, four primary care physicians, and three surgical specialists. Most of these physicians were evaluated by a psychologist who is expert in the diagnosis and treatment of sexual problems.

One case resulted in a license revocation and another in the physician's retirement in lieu of board sanction. One involved a decade-old case that came to the board's attention through self-report. The remaining eight cases resulted in suspensions from practice extending up to 3 months and fines up to \$5,000, the most that the board can levy under the law. Seven physicians were placed on probation, and all were referred to a therapy program. In addition, four other physicians were sent letters of concern regarding inappropriate examination practices with sexual overtones.

A combination of temporary suspension, fine, probation, and therapy is now the typical disposition adopted by the board in such cases. These sanctions may be modified by aggravating or mitigating factors in individual cases. Revocation of the license remains a consideration for the most serious situations.

DISCUSSION

This article has described the varied components of 12 years of continuous psychiatric consultation to the Oregon Board of Medical Examiners. We believe that the psychiatric consultant has helped the board understand the psychiatric aspects of many individual cases. The Oregon board maintains a major interest in rehabilitating physicians, and the consultant has a defined role in working with the board and the board staff in the development of intervention programs for the problems described in this report. In addition, the consultant has a key role in helping the board develop a research agenda focused on the physician problems brought before the board. The focus on both rehabilitation and research has led to the development of organized intervention programs in each of the categories of physician impairment we have described. Each category presents unique and challenging rehabilitation problems, which we now discuss briefly along with future research directions for each.

Where medical boards and organized medicine collaborate in the identification, treatment, and rehabilitation of substance-abusing physicians, positive results can be expected. Monitored treatment programs have proven to be an effective means of satisfying the dual public policy goals of protection of the public and physician rehabilitation. Future research should concentrate on the relation between the board's mandates and diversion treatment programs as the attempt is made to intervene earlier, and on a voluntary basis, with substance-abusing physicians.

The most common mental illness that comes to the attention of the board is represented by physicians with bipolar illness who have demonstrated significant problems in judgment associated with elevated mood.

Again, a monitored treatment approach has produced positive outcomes for these physicians. Treatment is provided by practicing psychiatrists who are willing to see these physicians and report to the board on a regular basis. Research in this area could further elucidate the potential effectiveness of mandated treatment for mental illness (21).

There is also an important issue of confidentiality in relation to physicians who have experienced mental health treatment in the past. The Oregon board has taken the position that it should be made aware of the previous mental health treatment of those who apply for licenses and any new courses of treatment for those who are already licensed. This stance allows the board to review the facts of individual situations to determine whether there is concern about a physician's ability to practice medicine safely. This inquiry into a physician's past psychiatric treatment challenges the board's ability to review psychiatric information in a manner that guards against stigmatizing physicians who have been in psychiatric treatment but present few if any concerns regarding their ability to practice medicine. Guidelines have been developed for identifying factors that might increase the board's concern about practicing physicians. Previous psychiatric hospitalization is one important factor stimulating further inquiry and/or psychiatric evaluation.

The third area of concern to psychiatric consultation is inappropriate prescribing and chronic pain. This is an area of national concern in which psychiatrists, especially those interested in consultation/liaison psychiatry and the treatment of chronic pain, have made contributions (22). Extending psychiatric consultation to the physicians brought before a medical board for inappropriate prescribing is an extension of concern for the chronic pain patient. Identifying emotional factors that underlie some inappropriate prescribing practices extends the area of interest from a focus on the rational management of the chronic pain patient to the physician's characteristics and the emotional factors which influence the decision to prescribe. To prescribe medication is a powerful right of physicians. It has become clear that in addition to having the requisite knowledge for prescribing, physicians need to be more familiar with the emotional aspects of the act of prescribing and the nature of the physician-patient interaction. Future research should focus on the effectiveness of intervention programs developed by the board to address these issues.

The fourth focus for psychiatric consultation relates to the sexual abuse of patients. This is a problem of growing national importance. Consistent with its approach in other areas, the board has taken the position that there is a place for rehabilitation of offending physicians. From a more general perspective, these cases are currently addressed in Oregon by the board, the ethics committees of professional organizations, institutional disciplinary committees, and tort law. We believe that among these regulatory bodies, ethics committees, and the civil law there are enough options to handle this

problem. The passage of criminal statutes with respect to the problem, as has been done in several jurisdictions (23), further complicates a very difficult situation. Future research might focus on the development of conceptual models for the evaluation and treatment of physicians involved in the sexual abuse of patients.

The focus on problems of inappropriate prescribing and sexual abuse of patients has reemphasized the fundamental importance of the physician-patient relationship. In both of these areas psychological vulnerabilities can lead to a relationship between physician and patient that is destructive rather than therapeutic. Both types of problems can have profoundly negative effects on patients. Both involve issues of physician-patient boundaries, difficulties with limit setting, and physician characteristics such as paternalism, need to rescue, grandiosity, and countertransference. Some nonpsychiatric physicians have told us that they never thought about the physician-patient relationship in any meaningful way until after they were in deep trouble. They had never conceptualized ideas about transference and countertransference, and they had no way of meaningfully assessing the emotional needs of their patients. This is an issue that we believe calls for significant program development both in medical schools and for practicing physicians.

We have presented an overview of psychiatric consultation to one medical board. As in any consultation, we are dealing with a dynamic process in which the group process of the board and the interplay between board, staff, and consultant determines outcome. We are not claiming that we have a perfect system, but we do view the consultation as successful in helping the board carry out its mandated functions, as well as in developing programs that are responsive to newly identified areas of physician impairment. Given the complicated tasks faced by medical boards, the program developed in Oregon should be of interest to other jurisdictions.

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The Comorbidity of Borderline Personality Disorder and Other *DSM-III-R* Axis II Personality Disorders

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Objective: This study examines the comorbidity of *DSM-III-R* borderline personality disorder and the other axis II personality disorders. The extent and direction of overlap provides a measure of the clarity of its diagnostic boundaries and descriptive validity. **Method:** In 110 outpatients without concurrent major axis I conditions, axis II diagnoses were assessed in semistructured format and all *DSM-III-R* personality disorder criteria were rated. Multiple diagnoses were recorded. **Results:** Twenty-two patients (20%) met criteria for borderline personality disorder; 18 (82%) had at least one additional personality disorder diagnosis. Using measures of frequencies and intercorrelation coefficients, the authors found that overlap was extensive and not confined to any one of the three designated axis II clusters. Factor analysis revealed 1) a group containing borderline personality disorder with paranoid, histrionic, narcissistic, antisocial, and passive-aggressive personality disorders and 2) another grouping of schizoid, schizotypal, avoidant, obsessive-compulsive, and self-defeating personality disorders. **Conclusions:** Borderline personality disorder appears to constitute a broad, heterogeneous category with unclear boundaries that embraces a general personality disorder concept. Both further refinement of the borderline personality disorder construct and investigation into alternative models to the *DSM-III-R* axis II classification system are suggested.

(*Am J Psychiatry* 1991; 148:1371-1377)

Since its inclusion in *DSM-III*, borderline personality disorder has become the most extensively studied and frequently diagnosed personality disorder. Empirical studies, using systematic assessment techniques, consistently demonstrate that borderline personality disorder substantially overlaps other personality disorder diagnoses and is rarely the only one present. In clinical practice, however, even though axis II categories are permitted to overlap, making it possible to diagnose complex personality disturbance, multiple diagnoses are rare. In part because clinicians seem to view personality as a single integrated system of interrelated parts, they find multiple diagnoses conceptually unsatisfying (1) and usually assign only one personality disorder diagnosis to a patient (2). This divergence of clinical application from the assignment strategy of *DSM-III-R* is certainly a contributory factor to the findings of poor

reliability of clinically based personality diagnoses. The study of the comorbidity of borderline personality disorder and other personality disorders deserves further attention in order to refine the borderline personality disorder construct and to determine whether alternative diagnostic systems are capable of more parsimonious data integration.

DSM-III-R establishes a prototypal categorical model of classification using intentional polythetic definitions for the axis II taxa. Categorical differences and comorbidity between hypothetical constructs with fallible indicators are assumed. The minimum of five of eight criteria algorithm for borderline personality disorder allows for 93 combinations and membership heterogeneity. Because members are heterogeneous with respect to defining criteria and may simultaneously meet those for other personality disorders, the demonstration of heterogeneity in relation to hypothesized covariates of a particular diagnosis should be expected (3). Any assumptions of homogeneity for the borderline construct within the prototypal system become questionable. Without an infallible biological criterion or precise definition, the determination of borderline personality disorder must rest on statistical proofs to establish a central covariant cluster of criteria that can demonstrate bimodality or a point of rarity with other

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The authors thank John Kane, M.D., and Arthur Rifkin, M.D., for their assistance.

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TABLE 1. Minor *DSM-III-R* Axis I Diagnoses for 110 Outpatients^a

Diagnosis	Number of Patients
Anxiety disorder	68
Panic disorder	20
Panic disorder and agoraphobia	10
Agoraphobia	1
Generalized anxiety disorder	23
Social phobia	11
Simple phobia	2
Atypical anxiety disorder	1
Mood disorder	23
Dysthymia	19
Atypical depression	3
Cyclothymia	1
Adjustment disorder	11
V code	5
Other	13
Somatoform disorder	7
Sexual disorder	3
Impulse disorder	1
Eating disorder	1
Brief reactive psychosis	1

^aMultiple diagnoses were recorded.

conditions. Therefore, findings suggestive of discontinuity between characteristics of borderline personality disorder and other personality disorders cannot exclude the possibility that the relevant data were drawn from two extremes of a single continuum. The set of criteria for borderline personality disorder can be indicative of a discrete diagnostic entity; a nonspecific entity overlapping other disorders along a spectrum of impulsive, affective, and anxious pathologies; or additional symptoms within a complex syndrome (4).

The purpose of this study was to examine the extent and direction of the comorbidity of borderline and other personality disorders. This can serve to provide some measure of the character of its boundaries, heterogeneity, and descriptive validity. The hypothesis was that borderline personality disorder would demonstrate wide overlap and covariation with other personality disorder categories, extending beyond its specified dramatic "B" cluster, which does not support categorical distinction.

METHOD

The study subjects were 110 outpatients without concurrent major *DSM-III-R* axis I diagnoses. Details regarding recruitment, diagnosis, and procedure are presented elsewhere (4). Inclusion criteria were restricted to any minor axis I diagnosis—anxiety, dysthymia, other nonmajor mood, adjustment, V code, somatoform, sexual, dissociative, factitious, impulse, or eating disorder, brief reactive psychosis, other nonpsychotic grouping, or no axis I disorder. Brief reactive psychosis was included in this group because it is transient, usually secondary to a preexisting personality disorder, and requires that the more pervasive disorders considered in the major axis I grouping be ruled out. Exclu-

sionary criteria were diagnosis of schizophrenia, schizoaffective disorder, major affective disorder, delusional disorder, organic disorder, mental retardation, and alcohol or drug addiction.

The subjects' ages ranged from 18 to 60 years (mean \pm SD = 35 \pm 9). The mean sample age is consistent with comparable studies (5–7). There were 49 men (45%) and 61 women (55%). All assigned axis I diagnoses were confirmed to meet *DSM-III-R* criteria and consisted primarily of anxiety (56%) and dysthymic mood spectrum (35%) disorders (table 1).

Axis II diagnostic criteria ratings were determined by experienced clinicians with extensive training in the diagnosis of personality disorders and the use of the instruments. To minimize the effect of acute state conditions on personality measurement, subjects completed 6 months of treatment for inclusion in the study. Following the LEAD (longitudinal, expert, and all data) standard (8), the assessment was conducted openly according to the interviewers' style of obtaining all the required data over time from multiple sources (e.g., patient, chart, significant others, former clinicians). This method for obtaining a comprehensive, longitudinal clinical assessment reportedly improves reliability and accuracy in clinical diagnosis and provides a more optimal database for making the best possible diagnosis. Since the essence of personality disorders is maladaptive behavior or traits characteristic of long-term functioning not limited to the episode of illness, the LEAD standard seemed appropriate for this study. It has more observer variance than a structured instrument but also has less subject and occasion variance.

The ratings for the semistructured assessment were recorded on an inventory that listed each of the 112 *DSM-III-R* criteria for each of the personality categories (with self-defeating). Every item must be scored as explicitly present or absent. To offset clinician bias and increase reliability, there were a number of training sessions in the use of the instrument. For the study, each rater generated an independent rating of symptoms and diagnoses with supporting documentation for each patient on the basis of thorough clinical interviews and other acquired information. A personality diagnosis was rated as present if the minimal required criteria were scored at threshold. Multiple diagnoses were recorded.

To establish a measure of reliability for the ratings of the personality disorder criteria (dimensional measure) and diagnoses (categorical measure), an independent rater blind to the patients' diagnoses administered the Structured Interview for *DSM-III* Personality Disorders (9) to a randomly selected sample (10%) of the patients. To calculate diagnostic consistency across instrument measures is a recognized compromise solution. It was chosen because the individual items on the structured interview correspond to the individual *DSM-III-R* personality disorder criteria listed in the inventory, and a second independent, in-depth clinical rating for replication on each patient was not feasible, since the patients were so well known to those who rated and treated

TABLE 2. Base Rate, Reliability, and Number of Symptoms of Personality Disorders in 110 Outpatients

Personality Disorder	Number of Patients	Base Rate	Patients Without Other Personality Disorders		K	Yule's Y	Number of Symptoms		
			N	%			Maximum	Mean	SD
Paranoid	14	0.13	2	14	0.78	0.80	7	1.15	1.71
Schizoid	4	0.04	2	50	0.82	1.00	7	0.64	1.11
Schizotypal	3	0.03	0	0	0.75	0.83	9	0.75	1.22
Histrionic	19	0.17	4	21	0.47	0.57	8	1.38	1.95
Narcissistic	18	0.16	2	11	0.60	0.63	9	1.97	2.34
Antisocial	2	0.02	0	0	0.61	0.64	22	0.82	2.10
Borderline	22	0.20	4	18	0.72	0.72	8	2.33	2.13
Avoidant	26	0.24	8	31	0.59	0.61	7	2.26	1.78
Dependent	18	0.16	4	24	0.35	0.36	9	2.45	1.81
Obsessive-compulsive	6	0.05	1	17	0.66	0.76	9	1.48	1.68
Passive-aggressive	8	0.07	0	0	0.43	0.47	9	1.38	1.93
Self-defeating	15	0.14	5	33	0.56	0.58	8	2.18	2.04

them. Differences in criteria and diagnoses ratings between the cross-sectional structured interview measure and the longitudinal semistructured clinical *DSM-III-R* inventory measure technically measure concurrent validity rather than rater error. To obtain a measure of rating reliability between the two instruments, we focused on the individual criteria obtained by both instruments. The blind rater who administered the structured interview transposed those ratings to the *DSM-III-R* personality disorder inventory to derive corresponding ratings for the 112 items. The individual criteria ratings of the inventory generated by the structured interview and the semistructured clinical *DSM-III-R* inventory were then used to calculate agreement; the overall kappa and Yule (Y) values, determined by summing all individual criteria and diagnoses, were 0.62 and 0.64, respectively, for all personality disorder criteria and 0.64 and 0.71 for all personality disorder diagnoses.

To remain consistent with the standard applied in previous studies (10) for identifying borderline patients, study subjects were rated independently with the Diagnostic Interview for Borderlines (11) to confirm the borderline personality disorder diagnosis. Inclusion in the borderline personality disorder group required a score of 7 or higher and a diagnosis of borderline personality disorder (five or more criteria) according to the clinical *DSM-III-R* semistructured inventory.

RESULTS

Sixty-eight patients (62%) had an axis II personality disorder diagnosis; 22 (20%) had borderline personality disorder, 46 (42%) had other personality disorder diagnoses, and 42 (38%) did not meet a sufficient number of criteria for a diagnosis of a specific personality disorder. The patients without a specific personality disorder diagnosis met a substantial number of criteria for personality disorders. Eighty (73%) of the total 110 patients and 58 (66%) of the 88 nonborderline patients met at least one criterion for borderline personality dis-

order. Personality disorder was not usually diagnosed alone. There were a total of 154 personality disorder diagnoses among the 68 patients with personality disorder. Multiple axis II diagnoses were present in 37 (54%) of the patients with personality disorder (mean number of diagnoses=2.3 per patient), 18 (82%) of the patients with borderline personality disorder (3.7 per patient) and 19 (41%) of the patients with other personality disorders (1.6 per patient) ($p<0.001$). The intercorrelation matrix of the axis II scores demonstrated extensive significant correlations (full data available from the authors on request). These distributions are consistent with other studies that identify borderline personality disorder among comparable samples in which axis I and axis II diagnoses were reported (1, 5-7, 12-22).

Table 2 presents the base rate, reliability, and mean number of symptoms for each of the personality disorders. The most prevalent personality disorder diagnoses were avoidant, borderline, histrionic, narcissistic, dependent, self-defeating, and paranoid (24%-13%). The high prevalence of avoidant personality disorder can be expected in this study sample with such a substantial base rate (56%) of panic and other anxiety disorders (15). Antisocial, schizotypal, schizoid, obsessive-compulsive and passive-aggressive personality disorders were less frequent (2%-7%). The Yule (Y) statistic is given in addition to kappa as a measure of interrater reliability. While both correct for chance agreement, the former is reportedly less dependent on the base rate in the particular population under study (23) but is more likely to overstate true reliability (24). As the standard reliability statistic, kappa's important practical feature is its interpretability in qualitative as well as quantitative terms. Therefore, we follow the suggestion of reporting both measures of association (25). These values are at levels comparable to those of other studies that address questions of axis II comorbidity (12). The dimensional aspect of personality disorder symptoms is indicated by the mean number of symptoms recorded for each personality disorder in the study sample. Al-

TABLE 3. Comorbidity and Intercorrelation of Symptoms and Diagnosis of Each Personality Disorder With Borderline Personality Disorder (N=22) in 110 Outpatients^a

Personality Disorder	Patients		Sensitivity	Specificity	Predictive Power		Chi-Square Analysis of Overlap ^b (df=1)		Correlation Coefficient (r)	
	N	%			Positive	Negative	χ^2	p	Symptoms	Diagnosis
Paranoid	14	13	0.41	0.94	0.64	0.86	19.66	<0.0001	0.56 ^c	0.42 ^c
Schizoid	4	4	0.05	0.97	0.25	0.80	0.15	n.s.	0.01	0.02
Schizotypal	3	3	0.09	0.99	0.67	0.81	1.73	n.s.	0.28 ^d	0.20
Histrionic	19	17	0.36	0.88	0.42	0.85	7.01	<0.01	0.40 ^c	0.25 ^d
Narcissistic	18	16	0.45	0.91	0.56	0.87	17.01	<0.0001	0.58 ^c	0.39 ^c
Antisocial	2	2	0.00	0.98	0.00	0.80	0.51	n.s.	0.42 ^c	0.07
Avoidant	26	24	0.32	0.78	0.27	0.82	1.02	n.s.	0.19	0.10
Dependent	18	16	0.41	0.90	0.50	0.86	12.11	<0.001	0.43 ^c	0.33 ^c
Obsessive-compulsive	6	5	0.18	0.98	0.67	0.83	8.64	<0.01	0.18	0.28 ^d
Passive-aggressive	8	7	0.27	0.98	0.75	0.84	16.31	<0.0001	0.54 ^c	0.39 ^c
Self-defeating	15	14	0.14	0.86	0.20	0.80	0.12	n.s.	0.23	0.00

^aThe table should be read as follows: 41% of borderline subjects also had paranoid personality disorder; 94% of nonborderline subjects did not have paranoid personality disorder; 64% of subjects with paranoid personality disorder also had borderline personality disorder; 86% of nonparanoid personality disorder subjects were also nonborderline. The difference in frequency of overlap was significant ($p < 0.0001$, chi-square analysis); the proportions of variance in personality disorder symptoms (dimension) and diagnosis (category) were 0.56 and 0.42, respectively; these measures of common variance were both significant at the level of confidence.

^bDetermined by 2×2 analysis (Yates' correction as indicated), with Bonferroni application for multiple comparisons.

^c $p < 0.001$, two-tailed.

^d $p < 0.01$, two-tailed.

though some of the disorders were infrequent, a substantial proportion of each disorder's symptoms was often present.

Table 3 shows the comorbidity and intercorrelation of symptoms and diagnosis of each personality disorder with borderline personality disorder. The frequency and direction of overlap are presented in terms of sensitivity, specificity, and positive and negative predictive power. Sensitivity and specificity values express the frequency of the presence or absence of the individual personality disorder given the presence or absence, respectively, of borderline personality disorder. Positive and negative predictive power give the converse, that is, the frequency of the presence or absence of borderline personality disorder given the presence or absence, respectively, of the other individual personality disorder. It is to be noted that since predictive power values are influenced by base rates in the population studied, they are more likely to vary than sensitivity and specificity. An overlap of positive predictive power of 0.50 or more with borderline was found for paranoid, schizotypal, narcissistic, dependent, obsessive-compulsive, and passive-aggressive personality disorders. With the exception of schizotypal disorder, these values attained statistical significance. Overlap with histrionic personality disorder was somewhat lower but still significant at 0.42. Schizoid, antisocial, avoidant, and self-defeating personality disorders demonstrated less nonsignificant overlap with borderline personality disorder (positive predictive power of 0.27 or less). However, the strength of relationship between two variables is not measured just by statistical significance of the difference in frequencies. That only indicates how unlikely the co-occurrence happens by chance. Strength of association is more accurately measured by common variance, that is, the proportion of variance in one condition that is as-

sociated with the other. Significance of intercorrelation coefficients (covariation) was extensive, and it varied according to dimensional or categorical analysis of the scores. None was above 0.60.

Factor analysis was performed on the full derived intercorrelation matrix by using the Statistical Package for the Social Sciences program (26). With squared multiple correlations as communality estimates, principal factors were extracted and rotated to an orthogonal solution by the varimax procedure. Two factors were generated with eigenvalues greater than 1 and accounted for 69% of the variance. The standardized factor coefficients for each variable are summarized in table 4. The first factor contains borderline personality disorder with paranoid, histrionic, narcissistic, antisocial, and passive-aggressive personality disorders. The second factor includes schizoid, schizotypal, avoidant, obsessive-compulsive, and self-defeating personality disorders. The factor coefficients for dependent personality disorder were less than 0.4 and therefore were loaded in neither factor. It is to be noted that dependent personality disorder also demonstrated additional broad overlap with other categories, e.g., with avoidant personality disorder (47%); this replicates a similar finding reported by Trull et al. (27).

DISCUSSION

Insufficient attention has been paid to the fact that every study of borderline personality disorder finds substantial and variable overlap with other psychiatric diagnoses (19). Twelve reports in the prevailing literature provide data on the concurrence of all the other axis II personality disorder categories and borderline personality disorder (1, 5, 7, 12, 28-35); nine (5, 12,

TABLE 4. Standardized Factor Coefficients for Factor Analysis of Ratings for *DSM-III-R* Personality Disorders for 110 Outpatients

Personality Disorder	Standardized Factor Coefficient ^a	
	Factor 1	Factor 2
Paranoid	0.68	0.21
Schizoid	-0.14	0.50
Schizotypal	0.18	0.56
Histrionic	0.74	-0.07
Narcissistic	0.93	0.05
Antisocial	0.55	-0.02
Borderline	0.66	0.26
Avoidant	0.05	0.76
Dependent	0.34	0.33
Obsessive-compulsive	0.25	0.47
Passive-aggressive	0.79	0.20
Self-defeating	0.06	0.42

^aFactors 1 and 2 accounted for 44% and 25% of the variance, respectively. Factor 1 consisted of borderline, paranoid, histrionic, narcissistic, antisocial, and passive-aggressive personality disorders. Factor 2 consisted of schizoid, schizotypal, avoidant, obsessive-compulsive, and self-defeating personality disorders.

28–31, 33–35) present frequencies of each for the other, three (1, 7, 33) give intercorrelation matrices, and two (1, 32) contain factor analyses. None presents all the measures together. The substantial variation among the findings is to be expected, reflecting differences in samples (five inpatient, four outpatient, one nonpatient), base rates, control groups, assessment methods, diagnostic instruments, ascertainment factors, precision, capitalization on chance, data management, and *DSM-III* version used. Statistics of correlation, which assume linear relationships, may speciously suggest comorbidity because diagnostic criteria may be shared. While the overall rate of personality disorders in a sample may be substantial, the rates of some of the individual disorders are frequently low. Type II error, or false acceptance of the null hypothesis, must not be overlooked. These considerations also apply to this study and require caution in the interpretation of the findings.

The results of this study to systematically examine the comorbidity of *DSM-III-R* borderline personality disorder and the other axis II personality disorders with measures of frequencies, intercorrelation coefficients, and factor analysis indicate that given the presence of borderline personality disorder, multiple personality disorder diagnoses are the rule rather than the exception. Overlap is broad and not confined to any one of the three category clusters (odd, dramatic, anxious). The measures of interrelationship vary according to the method of analysis, whether the database is handled categorically or dimensionally, and the effect of the base rates of the individual disorders on the correlational and conditional probability statistics. Significant categorical association between borderline and paranoid, histrionic, narcissistic, dependent, obsessive-compulsive, or passive-aggressive personality disorder broadened, when considered dimensionally, to include antisocial and schizotypal personality disorders. The categorical system loses some statistical power because patients can share a substantial number of features

without meeting the required number of criteria necessary for the diagnosis. Although statistically significant, none of the correlations or frequencies of codiagnosis permits interchangeability.

Factor analysis provides an additional measure of association in emphasizing similarities or redundancies by combining closely correlated variables. This yielded two groups. The borderline group associated with their own second “dramatic” cluster (narcissistic, histrionic, antisocial) and both first “odd” (paranoid) and third “anxious” (passive-aggressive) clusters. This lack of association with any specific cluster category does not provide support for the hierarchical organization of the personality disorders into the current *DSM-III-R* clusters (36). The second non-borderline factor, which contains the schizoid, schizotypal, avoidant, obsessive-compulsive, and self-defeating categories, not unexpectedly reflects the schizoid realm that existed before *DSM-III*. Such persons characterized as aloof, emotionally detached, fearful, competition avoidant, having difficulty expressing anger, and occasionally eccentric, were subdivided into the schizoid, schizotypal, and avoidant categories of the current system (37). As shown in a number of studies, while these patients may demonstrate an overlap in positive criteria with borderline personality disorder (5, 7, 28–31, 36), factor analysis separates them into different dimensions within a general personality disorder construct (1, 32; *DSM-III-R*). Although factor analysis can determine the number of dimensions present, it is limited by the fact that behavioral variation may differ from the underlying biogenetic structure. Extra statistical information is required to specify the structure of the underlying biological and social variability in personality disorders (38).

Covariation and differentiation are not mutually exclusive concepts. Covariation refers to the fact that patients having one disorder also meet criteria for additional diagnoses. This can occur either because of comorbidity or as an artifact of overlapping criteria meanings (36). To the extent that personality disorder diagnoses are based on overlapping symptoms, the apparent presence of two or more concurrent disorders may actually be one disorder that has been given two or more diagnoses (39). It appears that borderline personality disorder, while demonstrating significant covariation, can to varying degrees be distinguished from other personality disorder categories and placed in different dimensions within the overall personality disorder construct (40, 41). The extensive overlap can therefore suggest that borderline personality disorder embraces a general personality disorder concept which is a significant component among a number of different disorders.

It must be underscored that this study does not propose that the identified significance and strength of association between borderline and other personality disorders be taken as definitive, but rather as an additional empirical contribution to the study of the heterogeneity and diagnostic boundaries of patients who would be considered to have borderline personality disorder. Although the methodological limitations to generalizabil-

ity must render conclusions tentative, the data are believable and provide a basis for further hypothesis testing. Validation studies will require large patient and nonpatient samples to further determine the distinctiveness of the individual disorders. Multicenter collaborative studies seem to be particularly indicated for this task. The methodological issues notwithstanding, there remains a consistency to the findings of variability across studies that may be the salient issue, reflecting the protean or inchoate nature of the borderline personality disorder construct itself.

At the risk of going beyond the database, the comorbidity findings for borderline personality disorder suggest further considerations regarding the *DSM-III-R* axis II classification system. Can the current categorical system of 13 disorders be supported over alternative models establishing variants (dimensions) or subtypes of a larger general personality disorder or spectrum construct (33)? According to Kendell and Brockington (42), the persistent failure to find discontinuities between symptoms and outcome suggests that the mental disorders may be best conceptualized as continuous variations of symptoms and perhaps etiologies as well. Rutter (43) finds little justification for the retention of current trait-defined personality disorders. Although traits may be useful descriptors, they are dimensional, not categorical, terms. The work of Meehl (44) and Holzman (45) suggests that personality disorder can represent a phenotypic expression of a genetically transmitted, latent taxon or trait along a spectrum of pathology leading to axis I conditions, e.g., schizogene → schizotaxic defect → schizotypal personality disorder → clinical schizophrenia. Since the predisposition interacts across time with a complex variety of sociologic, intrapersonal, interpersonal, familial, cognitive, and other genetic variables, the presence of the genotype can be categorical, while the phenotype(s) may be dimensional (39). Therefore, it may be more informative to examine causal influences or other covariates according to different dimensions or components of a disorder (46). Empirical data showing that neurobiological variables may correlate better with character traits than specific diagnostic categories are available (47). Further refinement of axis II and more isomorphic measures of trait and diagnosis are needed to test new models and decide which system, dimensional or categorical, works best.

CONCLUSIONS

This study, consistent with the literature for axis I comorbidity (19), suggests that patients who meet *DSM-III-R* criteria for borderline personality disorder constitute a very heterogeneous group with unclear boundaries whose overlap with neighboring personality disorder categories is extensive. The orthogonal dimensional nature of personality structure provides three explanations for the comorbidity phenomena of borderline personality disorder (48). 1) The personality

disorders are located on different orthogonal dimensions and are independent of each other. 2) Borderline personality disorder and the other personality disorders are located on the same dimension, and one is more extreme than the other. 3) Borderline personality disorder and the other personality disorders contain highly correlated traits from the same dimension and are features of the same disorder. To add to the complexity, more than one may apply. A better understanding of personality disorder awaits a paradigmatic shift away from discrete nosologic categories to alternative models that recognize that pathology can cross conceptual borders of nosologic categories, reject a priori assumptions of unitary syndromes, and endorse the concept of complexly regulated syndrome clusters common to multiple diagnostic categories.

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Affective and Impulsive Personality Disorder Traits in the Relatives of Patients With Borderline Personality Disorder

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Objective: This study tested the hypothesis that the risk for affective and impulsive personality disorder traits commonly found in patients with borderline personality disorder would be greater in the first-degree relatives of probands with borderline personality disorder than in two comparison groups. **Method:** Blind family history interviews were conducted with family informants to assess the extent to which first-degree relatives of 29 probands with borderline personality disorder, 22 probands with other personality disorders who met three or fewer of the criteria for borderline personality disorder, and 43 probands with schizophrenia fulfilled operationalized criteria for the two kinds of personality disorder traits and for other diagnostic categories. The crude proportions of adult relatives with each diagnosis, as well as the age-adjusted morbid risks, were assessed in the three groups of relatives. **Results:** The risks for affective and impulsive personality disorder traits were independently greater in the 129 relatives of the borderline probands than in the 105 relatives of the probands with other personality disorders and the 218 relatives of the schizophrenic probands. There was no similarly greater risk for any other psychiatric disorder assessed, including major affective disorder. In addition, the relatives of borderline probands with current or past major depressive disorder showed a greater risk for major affective disorders than the relatives of never-depressed probands with other personality disorders but not the relatives of never-depressed borderline probands. **Conclusions:** These results suggest familial transmission of the hallmark borderline-related personality characteristics and raise the possibility that these familial traits may be partially independent.

(Am J Psychiatry 1991; 148:1378-1385)

Borderline personality disorder has been previously hypothesized to have a familial relation to major affective disorder (1-5). However, most of the more recent studies of familial association between these two disorders have found a significant relationship only when the proband with borderline personality disorder had a comorbid diagnosis of major depressive disorder (6, 7). It has been suggested that there is familial aggregation of borderline personality disorder, prominent borderline personality traits, and personality disorders with related personality traits (e.g., histrionic and anti-

social personality disorders, which share with borderline personality disorder affective instability and impulsivity, respectively); this suggestion followed the observation of greater frequency of borderline personality disorder and borderline-related personality disorders among relatives of probands with borderline personality disorder (6-10).

Evidence consistent with the familial transmission of borderline characteristics may stem from a *dimensional* model of borderline personality disorder, in which several relatively distinct borderline-related temperamental factors aggregate in families, rather than a *categorical* model, in which borderline personality disorder is conceptualized as a discrete syndrome. Heuristically, such dimensions appear to be better candidates for transmissible psychobiologic substrates (11) than the more complex constellation of these traits and the other symptoms that are found together in the *DSM-III* criteria for borderline personality disorder. These substrates may then evolve through developmental factors into the personality traits observed in patients with bor-

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Supported by a Schizophrenia Biological Research Center grant from the VA Medical Research Service, NIMH merit review award MH-42827 to Dr. Siever, and an NIMH program project grant for cellular and molecular markers in schizophrenia.

derline personality disorder. Included among them may be impaired affective regulation and poor impulse control, which underlie the hallmark traits associated with borderline personality disorder: affective instability and impulsivity (5, 6, 11). Such a model would lead to the prediction that relatives of patients with borderline personality disorder will have high levels of both impulsivity and affective instability but that these traits need not occur together in the same relatives.

In the present study, family history criteria were established to identify chronic affective instability and chronic impulsivity, and the morbid risks for these traits and other disorders were assessed in relatives of patients with borderline personality disorder and in relatives of patients with other personality disorders. Our major hypothesis was that both affective and impulsive personality traits would be independently greater in the relatives of the borderline probands than in the relatives of clearly nonborderline probands with other personality disorders. In addition, we assessed the impact of a comorbid diagnosis of major depression in both sets of probands on the prevalence of major affective disorders in their relatives. Finally, as a subsidiary analysis, we compared the risks for the relatives of the probands with borderline personality disorder to the risks for the relatives of a group of schizophrenic probands.

METHOD

All probands in this study provided informed consent and were recruited on the basis of consecutive hospital admissions and without reference to family history status.

Family history information was obtained from informants for 64 probands with personality disorders. Most of the probands ($N=58$) were male, and their mean \pm SD age was 37.9 \pm 10.2 years (range=21–63). They were participating in a study of biological correlates of personality disorders at the Bronx Veterans Administration (VA) and Mount Sinai medical centers and were invited to participate if, upon clinical assessment, they had a primary clinical diagnosis of personality disorder. The Schedule for Affective Disorders and Schizophrenia (SADS) (12) was administered to the probands by one or two interviewers to assess the presence of Research Diagnostic Criteria (RDC) and *DSM-III* axis I disorders; interrater reliability for major depressive disorder was good ($\kappa=0.93$).

Patients meeting the criteria for a personality disorder who also met the criteria for any psychotic disorder, including schizophrenia, schizoaffective disorder, bipolar disorder, and schizophreniform disorder, or for alcoholism or substance abuse/dependence in the past 6 months were excluded from the study. These exclusionary criteria were designed to help identify a group of primary personality disorder patients whose psychopathology was related to their primary, enduring maladaptive personality traits rather than secondary to psychosis or substance use. A current or past major de-

pressive disorder, however, was not an exclusion criterion for the study. This disorder frequently coexists in patients with personality disorders (13), and personality disorder traits were judged to be more readily identified as primary or secondary in such patients than in those with current substance abuse or psychotic disorders. However, in order for a patient to be included in the study as having a primary personality disorder, the personality disorder had to have preceded the other disorder and to have been the major source of ongoing occupational or social impairment, as determined by the diagnostic interview assessment. Patients with personality disorder traits confined to or following depressive episodes or periods of substance abuse were excluded. In addition, personality disorder assessments of such patients were routinely conducted after the symptoms of clinical depression had remitted.

The Structured Interview for the *DSM-III* Personality Disorders (14) was used to diagnose all *DSM-III* axis II personality disorders. One or two interviewers administered this interview to each proband ($\kappa=0.81$ for the diagnosis of borderline personality disorder). An additional independent interviewer used the interview with a knowledgeable informant. Discrepancies between patient and informant interviews were discussed, and a final consensus diagnosis was obtained for each proband at a diagnostic meeting conducted by a diagnostic expert (H.K. or T.B.H.). In 14 (22%) of the 64 cases, an axis II diagnosis was made without an informant interview.

Concurrent family history information was collected from informants for 43 male schizophrenic probands (mean \pm SD age=44.3 \pm 18.0 years) who had been consecutively admitted to the Schizophrenia Biological Research Center at the Bronx VA Medical Center. The diagnosis of schizophrenia according to the RDC with information obtained from the SADS was made at a consensus meeting between two raters and a diagnostic expert (T.B.H.) ($\kappa=0.86$ for the diagnosis of schizophrenia).

Family history interview methods have been described in detail elsewhere (15). Diagnostic information was collected, by persons blind to the probands' diagnoses, on all first-degree relatives of the probands, primarily through telephone interviews with knowledgeable informants, usually first-degree relatives or spouses. In five cases the probands themselves served as informants. The families of 57 (53%) of the 107 probands were assessed with the help of at least two informants. Upon breaking the blind, we found that a substantially larger proportion of the families of the schizophrenic probands (70%, $N=30$) than of the personality disorder probands (38%, $N=24$) had been assessed with two informants ($\chi^2=10.71$, $df=1$, $p<0.005$). In addition to assessments according to the Family History Research Diagnostic Criteria (FH-RDC) (16), data according to supplementary family history criteria for previously reported schizophrenia-related personality disorder traits (17) and for affective and impulsive personality disorder traits (appendix 1) were assessed.

TABLE 1. Age Structure Characteristics of First-Degree Relatives of Probands With Borderline Personality Disorder, Restrictive Other Personality Disorders,^a and Schizophrenia

Item	Relatives of Probands With Borderline Personality Disorder (N=129)	Relatives of Probands With Restrictive Other Personality Disorders (N=105)	Relatives of Probands With Schizophrenia (N=218)
Age (years)			
18–39	59	39	117
40–59	39	32	68
60 and over	31	34	33
Lifetimes of risk			
For major affective disorders ^b (period of risk: 18–59 years)	79	69	124.5
For other family history categories ^c (period of risk: 18–39 years)	98.5	85	158.5
Number of relatives in family ^d			
Mean	4.4	4.8	5.1
SD	1.8	3.1	2.7

^a“Restrictive other personality disorders” indicates *DSM-III* personality disorders with three or fewer borderline personality disorder traits.

^bIncludes depressive disorder, manic disorder, and acute schizoaffective disorder.

^cIncludes all other categories except antisocial personality disorder, which requires no age adjustment.

^dNo significant differences in mean family size were found.

Family history criteria for affective personality disorder traits were designed to characterize individuals with chronic affective instability not attributable to a concurrent major affective disorder. These criteria resemble the RDC for labile personality (18). Family history criteria for impulsive personality disorder traits were designed to characterize individuals with chronic impulsivity and are similar to the impulsivity criteria for borderline personality disorder and antisocial personality disorder.

A diagnosis was considered present in relatives who met criteria for at least a “probable” diagnosis. This diagnosis was assigned if there was any uncertainty about the relative’s meeting one, and only one, criterion in a diagnostic category. As described elsewhere (15), good interrater reliability was found for all the family history diagnostic categories, including the supplemental personality disorder trait categories and the category of no known disorder, assessed together in a 12×12 matrix ($\kappa=0.86$). In addition, interrater reliability was independently assessed for each of the supplementary personality disorder trait categories (rated present or absent) taken individually (affective personality disorder traits, $\kappa=1.00$; impulsive personality disorder traits, $\kappa=0.67$; schizophrenia-related personality traits, $\kappa=0.90$).

Two methods were used to assess familial aggregation: 1) the crude proportion, determined by dividing the number of identified cases by the raw number of adult relatives (i.e., those 18 years of age and older) and 2) the Weinberg Abridged Method (19), which adjusts the denominator used in the crude proportion by counting each relative considered to be still at risk for a given disorder as a half-lifetime of risk and each relative who has lived beyond the risk period as one lifetime of risk. We used an age of risk of 18–59 years for the major affective disorders and 18–39 years for the schizophrenia-related disorders, alcoholism, drug use disorder, and affective and impulsive personality disorder traits

(15, 17). Individuals older than 18 were considered to have lived through the age of risk for antisocial personality disorder.

Our major hypothesis was that both affective and impulsive personality disorder traits would be significantly greater in the relatives of the probands with borderline personality disorder than in the relatives of the probands who clearly lacked a borderline personality disorder diagnosis. The assessment of this hypothesis subsumed two major comparisons, each potentially contributing a component of support for it for each comparison group. For the statistical tests of these comparisons, the level of significance we used was $\alpha=0.05$, two-tailed. For comparisons not subsumed by our major hypothesis, we used the more stringent Bonferroni-corrected significance level, but we report results with and without correction for multiple comparisons.

RESULTS

Twenty-nine probands met the criteria for definite borderline personality disorder. Most of these probands also met criteria for other personality disorders: histrionic (N=18), schizotypal (N=12), compulsive (N=8), antisocial (N=6), paranoid (N=5), narcissistic (N=3), avoidant (N=3), and dependent (N=2). Thirty-five probands met the criteria for personality disorders other than borderline personality disorder. However, because 13 of the probands with these other personality disorders met four of the criteria for borderline personality disorder (i.e., only one less than required for the definite diagnosis of borderline personality disorder), we restricted the proband group with other personality disorders to include only those who met three or fewer of the criteria for borderline personality disorder and called this group “restrictive other personality disorders.” The personality disorder diagnoses in this group

TABLE 2. Morbid Risk and Crude Proportions of Psychiatric Disorders Among First-Degree Relatives of Probands With Borderline Personality Disorder, Restrictive Other Personality Disorders,^a and Schizophrenia

Family History Diagnosis	Relatives of Probands With Borderline Personality Disorder			Relatives of Probands With Restrictive Other Personality Disorders			Relatives of Probands With Schizophrenia		
	Cases	MR ^b	CP ^c	Cases	MR ^b	CP ^c	Cases	MR ^b	CP ^c
Affective personality disorder traits	17	0.173	0.132	3	0.035	0.029	13	0.082	0.060
Impulsive personality disorder traits	13	0.132	0.101	3	0.035	0.029	5	0.032	0.023
Depressive disorder	17	0.215	0.132	18	0.261	0.171	20	0.161	0.092
Manic disorder	2	0.025	0.016	1	0.014	0.010	0	0	0
Acute schizoaffective disorder	1	0.013	0.008	1	0.014	0.010	1	0.008	0.005
Major affective disorders	19	0.241	0.147	19	0.275	0.189	21	0.169	0.096
Chronic schizophrenia	1	0.010	0.008	0	0	0	4	0.025	0.018
Chronic schizoaffective disorder	1	0.010	0.008	0	0	0	2	0.013	0.009
Schizophrenia-related personality disorder	12	0.122	0.093	8	0.094	0.076	28	0.177	0.128
Schizophrenia spectrum disorders	14	0.142	0.109	8	0.094	0.076	34	0.215	0.156
Antisocial personality disorder ^d	4		0.031	4		0.038	7		0.032
Alcohol disorder	18	0.179	0.140	13	0.153	0.124	31	0.196	0.142
Drug use disorder	6	0.060	0.045	5	0.059	0.048	7	0.044	0.032

^a"Restrictive other personality disorders" indicates *DSM-III* personality disorders with three or fewer borderline personality disorder traits.

^bMR (morbid risk)=number of cases divided by age-adjusted lifetimes of risk.

^cCP (crude proportion)=number of cases divided by number of relatives 18 years of age or older.

^dNo age correction for this category.

were schizotypal (N=10), paranoid (N=8), compulsive (N=5), histrionic (N=4), avoidant (N=2), dependent (N=1), narcissistic (N=1), and mixed (N=1).

The mean±SD age of the borderline personality disorder probands (35.1±8.3 years) was not significantly different from that of the restrictive other personality disorder probands (38.4±10.3 years), nor were these groups significantly different in sex, marital status, or level of education. The relatives of 12 (41%) of the 29 borderline probands and seven (32%) of the 22 restrictive other personality disorder probands were assessed with two family informants ($\chi^2=2.81$, *df*=1, *n.s.*). The age structure and mean family size of the relatives in each group are shown in table 1. As indicated, no significant differences in family size between groups were observed.

Table 2 shows the numbers of relatives of the three proband groups who were given family history diagnoses for affective and impulsive personality disorder traits. In addition, the numbers of relatives in each of the other family history diagnostic categories are shown. Table 2 also indicates both the morbid risk according to the age-adjustment procedures (19) and the crude proportion of illness among all adult relatives.

Both the morbid risk and the crude proportion of affective personality disorder traits were significantly greater among the relatives of the probands with borderline personality disorder than among the relatives of the probands with restrictive other personality disorders (risk: $z=2.98$, $p<0.05$; proportion: $z=2.81$, $p<0.05$) and the relatives of the schizophrenic probands (risk: $z=2.31$, $p<0.05$; proportion: $z=2.20$, $p<0.05$). In addition, the morbid risk and the crude proportion of impulsive personality disorder traits were both significantly greater among the relatives of the borderline probands than among the relatives of the probands with restrictive other personality disorders (risk: $z=2.32$, $p<0.05$; proportion: $z=2.18$, $p<0.05$) and the

relatives of the schizophrenic probands (risk: $z=3.07$, $p<0.05$; proportion: $z=3.16$, $p<0.05$).

In contrast, neither method of assessing familial aggregation indicated significant differences between relatives of the borderline personality disorder probands and relatives of the two comparison proband groups for any other disorder assessed. This was true both with and without adjustments for multiple comparisons. Finally, no differences in the proportion or risk of affective or impulsive personality disorder traits were detected in comparisons of the relatives of the probands who had any other specific personality disorder diagnosis with the relatives of all other personality disorder probands (e.g., schizotypal versus nonschizotypal, histrionic versus nonhistrionic).

We observed little clustering of affective personality disorder or impulsive personality disorder traits within specific families. Excluding the proband, most cases of affective personality disorder traits (73%, N=24 of 33) and of impulsive personality disorder traits (77%, N=17 of 22) were identified in independent families. Furthermore, this overall absence of familial clustering was similar across the three proband groups (affective personality disorder traits: $\chi^2=2.12$, *df*=2, $p>0.30$; impulsive personality disorder traits: $\chi^2=2.43$, *df*=2, $p>0.30$).

Only four (8%) of the 50 relatives from the three proband groups who had either affective or impulsive personality disorder traits met the criteria for both kinds of traits. Three of these four were relatives of borderline personality disorder probands, and one was a relative of a schizophrenic proband ($\chi^2=4.34$, *df*=2, *n.s.*). In addition, there was no significant co-occurrence of these two disorders in relatives within the three proband groups. Thus, in each of the groups of relatives, affective and impulsive personality disorder traits seemed to emerge independently rather than concurrently.

TABLE 3. Morbid Risk and Crude Proportions of Major Affective Disorders Among First-Degree Relatives of Depressed and Nondepressed Probands With Borderline Personality Disorder and Other Personality Disorders^a

Family History Diagnosis	Relatives of Probands With Borderline Personality Disorder						Relatives of Probands With Other Personality Disorders					
	Depressed Probands			Nondepressed Probands			Depressed Probands			Nondepressed Probands		
	Cases	MR ^b	CP ^c	Cases	MR ^b	CP ^c	Cases	MR ^b	CP ^c	Cases	MR ^b	CP ^c
Depressive disorder	14	0.252	0.152	3	0.128	0.075	22	0.355	0.259	3	0.063	0.041
Manic disorder	2	0.036	0.022	0	0	0	2	0.032	0.024	0	0	0
Acute schizoaffective disorder	1	0.018	0.011	0	0	0	0	0	0	1	0.021	0.014
Major affective disorders	16	0.288	0.174	3	0.128	0.075	22	0.355	0.259	4	0.083	0.054

^aAge-adjusted lifetimes of risk and crude proportions of major affective disorders for relatives of the four proband groups: depressed borderline, lifetimes of risk=55.5, total relatives=92; nondepressed borderline, lifetimes of risk=23.5, total relatives=40; depressed other personality disorders, lifetimes of risk=62.0, total relatives=85; nondepressed other personality disorders, lifetimes of risk=48, total relatives=74.

^bMR (morbid risk)=number of cases divided by age-adjusted lifetimes of risk.

^cCP (crude proportion)=number of cases divided by number of relatives 18 years of age or older.

We further divided the borderline personality disorder and other personality disorder probands according to whether they had ever had a major depressive disorder, so as to test for possible greater familial risk for major affective disorders among depressed probands in the two groups. To maintain sufficient statistical power, all of the probands with other personality disorders, including the 13 who fulfilled four criteria for borderline personality disorder, were used in these analyses. Four proband groups were created: depressed borderline personality disorder (N=19), nondepressed borderline personality disorder (N=10), depressed other personality disorders (N=20), and nondepressed other personality disorders (N=15).

Table 3 shows the number of relatives in each of these subgroups who were given family history diagnoses for the major affective disorders taken individually and together in a single category and indicates the associated morbid risks and crude proportions. After Bonferroni correction for the six possible comparisons, the critical value for alpha, two-tailed, was 0.008. Neither the morbid risk nor the crude proportion of FH-RDC depressive disorder was significantly different in the relatives of the depressed borderline probands from that in the relatives of the nondepressed borderline probands, with or without the Bonferroni correction (risk: $z=1.23$, n.s.; proportion: $z=1.21$, n.s.). The morbid risk and crude proportion of depressive disorder were both marginally greater in the relatives of the depressed borderline probands (risk: $z=2.60$, $p=0.009$; proportion: $z=2.36$, $p=0.02$) and significantly greater in the relatives of the depressed other personality disorder probands (risk: $z=3.63$, $p<0.008$; proportion: $z=3.77$, $p<0.008$) than in the relatives of the nondepressed other personality disorder probands. The morbid risk and crude proportion of depressive disorder were also marginally greater in the relatives of the depressed other personality disorder probands than in the relatives of the nondepressed borderline probands (risk: $z=2.06$, $p=0.04$; proportion: $z=2.40$, $p=0.02$). Similar results were obtained in similar comparisons based on diagnosis of any

major affective disorder in relatives, although relatives with depressive disorder accounted for almost all (94%) of the major affective disorders identified.

DISCUSSION

These results raise the possibility that borderline personality disorder has a greater familial relation to two characteristic borderline-related personality traits, affective instability and impulsivity, than to the major affective disorders. Greater numbers of major affective disorders among relatives appeared instead to be primarily related to the comorbid diagnosis of depression in the personality disorder probands.

The results of this study are consistent with a model of borderline personality disorder conceptualized as issuing from the interaction of personality traits of impulsivity and affective instability. Although evidence for familial aggregation alone cannot distinguish between genetic and environmental factors, the data from this study support the possibility that these characteristics are transmitted in families and are at least partially distinct from each other or from familial associations of borderline personality disorder with the major affective disorders (11).

We found familial associations linking borderline personality disorder with both affective and impulsive personality disorder traits. Although these findings are in at least partial accord with those of the previous studies investigating borderline personality disorder in relatives, this is the first study that has investigated these two characteristics of borderline personality disorder as distinct and possibly independent personality traits. The relatively small degree of overlap of the two categories in the same relative raises at least the possibility that these traits have partially independent familial relations to borderline personality disorder. If so, the co-occurrence of these traits in an individual might contribute to the characteristic functioning found in patients with borderline personality disorder.

We chose not to evaluate in relatives every item associated with *DSM-III* borderline personality disorder, because the items reflecting an identity disturbance (item A4), an intolerance of being alone (item A6), and chronic feelings of emptiness and boredom (item A8) were considered to be too difficult to assess reliably through an informant's report. Furthermore, these symptoms, which appear grounded less on qualities of temperament than on the subjective, internal experience of self and the social/interpersonal world, were considered less likely to reflect directly the constitutional factors with biologic/genetic underpinnings (11). Thus, without having assessed the relatives with the full criteria for borderline personality disorder, we cannot definitively comment on the likely presence of borderline personality disorder among the relatives of probands with borderline personality disorder. However, only one previous study (7) found significantly greater proportions of relatives meeting the full *DSM-III* criteria for borderline personality disorder. Pope et al. (6), for example, found that just one of 130 relatives of borderline probands met the borderline personality disorder criteria; significant differences from relatives of psychiatric comparison groups were found only when the investigators included two additional dramatic cluster diagnoses: histrionic, featuring affective instability (e.g., *DSM-III-R* items 4 and 6) but not impulsivity, and antisocial personality disorder, featuring impulsivity (e.g., *DSM-III-R* items C3, C5, and C7) but not affective instability. Three other investigations (6, 8, 10) required less than the full borderline personality disorder criteria because of the probably weakened sensitivity of the family history method. This raises the possibility that some of the relatives assigned the borderline personality disorder diagnosis in previous studies would not have met the full criteria for *DSM-III* borderline personality disorder upon direct evaluation or, at least, would not have met the criteria associated with both chronic affective instability and impulsivity.

Our failure to find any significantly greater risk for other diagnoses among the relatives of probands with borderline personality disorder supports the hypothesis that these relatives' greater risk for affective and impulsive personality disorder traits is specific to these traits and is not the result of a generalized greater risk for psychopathology in these families.

These data provide some support for a dimensional model of borderline personality disorder, conceptualized as a clinical entity particularly reflecting the presence of two partially independent familial factors, chronic impulsivity and affective instability. Although environmental influences may play a role in accounting for these familial factors and, as noted, cannot be excluded on the basis of family diagnostic data, the results raise the possibility of a role for genetically heritable personality traits.

The major affective disorders were not more frequent among the relatives of the probands with borderline personality disorder than among the relatives of any of

the comparison groups, with or without correction for multiple comparisons. These findings are consistent with those of a twin study (20) and numerous earlier family and family history studies comparing relatives of borderline subjects with those of normal subjects (9), psychiatric control subjects (9, 21), and depressed probands (21). Furthermore, borderline personality disorder has not been found to be more frequent among the relatives of patients with major depression (22).

Investigations finding support for a relation between borderline personality disorder and the major affective disorders have also been reported (1-6), but many of these studies have lacked comparison samples (2, 3), had small sample sizes (1, 4), or failed to assess the role of major depression as a possible confounding factor (1-3, 6). In one recent study (5), however, contrary to the results of this study, relatives of borderline personality disorder probands did show a greater risk for affective disorders than relatives of schizophrenic patients. A reanalysis of those data, however, suggests that the difference in risk of depression between these groups was largely attributable to the relatives of depressed borderline probands ($p < 0.01$); only a trend toward greater risk was observed among the relatives of never-depressed borderline probands compared with the relatives of schizophrenic probands ($p = 0.06$).

The greater risk of major affective disorders in the relatives of depressed borderline personality disorder probands and depressed other personality disorder probands than in the relatives of nondepressed other personality disorder probands is consistent with the findings of earlier work (6, 9). It is important to note, however, that with or without correction for multiple comparisons, the risk of major affective disorders among the relatives of depressed borderline probands, though higher, was not significantly different from that observed among the relatives of nondepressed borderline probands. Our inability to detect statistical differences between these two groups thus leaves open the possibility of an attenuated familial relation between borderline personality disorder and the major affective disorders. Nevertheless, these results do not support a model of borderline personality disorder as simply a mild variant of the major affective disorders (2) or as a primary diagnostic entity that predisposes to episodes of exacerbation of major affective disorders (23). Although there may be a relation between affective instability and major depressive disorder, this trait appears to be at least partially independent of major depressive disorder as well.

The use of probands with other personality disorders as a comparison group for the group with borderline personality disorder potentially leaves a thin boundary between proband groups. For this reason, we drew comparisons with a more restrictive definition of other personality disorders to differentiate more clearly the two proband groups. The subsidiary use of schizophrenic probands provided an additional comparison with relatives of a proband group that had no apparent

relation to borderline personality disorder. However, the examination of probands with major affective disorders and no concurrent axis II diagnosis would further clarify the relation between the affective and impulsive personality disorder traits and the major affective disorders. In addition, the study of relatives of normal control subjects would help to determine whether the risk for these traits that we observed in the relatives of borderline probands is greater than the risk in the general population.

Comparing crude proportions of disorders between groups may tend to underestimate differentially the full risk to relatives by treating the status of relatives who are still at risk for a disorder as uncensored data. Alternatively, the Weinberg Abridged Method requires the specification of a period of risk, which may not be precisely known, and assumes a uniform risk across that period. To overcome partially the deficiencies of each of these methods, we assessed familial aggregation using both of them and found only minor differences in the significance levels of our results.

There is a potential for within-family correlations and differences between groups in mean family size to bias analyses in which family members from different groups are compared. In the present study, there was little within-family clustering for any of the proband groups. In addition, the average family size did not significantly differ for the different proband groups.

The presence of concurrent personality disorder diagnoses among borderline personality disorder probands raises the possibility that the results obtained for affective and impulsive personality disorder traits are related to these other personality disorders (e.g., histrionic or schizotypal). However, in ancillary analyses, the risks for affective and impulsive personality disorder traits were not significantly different among relatives of probands with any other specific personality disorder diagnosis and, in each case, among the relatives of personality disorder probands without that diagnosis.

The generalizability of this study's major findings must be limited to the families of patients in a hospital setting who have personality disorders without current substance abuse disorders. Furthermore, because a large proportion of the probands in this study were veterans, the proband sample was predominantly male, further limiting generalizability of the findings. Future studies might evaluate whether comparable familial aggregation is found in samples of borderline personality disorder probands of both sexes drawn from an unbiased, community-based population.

The use of the family history method also imposes limitations on the interpretation of these results. This method is inherently less comprehensive and accurate than the direct family study method. Most studies of the family history method have found that it possesses comparatively weak sensitivity but adequate specificity for commonly evaluated psychiatric disorders (16). We have recently examined preliminary data from an ongoing validity study of the family history criteria for affective personality disorder traits in which relatives evalu-

ated by family history interview have been reassessed in blind, direct family study interviews. To date, with a sample of 36 relatives of schizophrenic probands, affective personality disorder traits appear to possess good specificity (0.80) and sensitivity (0.73) for identifying affective instability (item 3 in *DSM-III-R* borderline personality disorder) (Silverman et al., unpublished data). Insufficient numbers of relatives with impulsive personality disorder traits ($N=3$) prevents a comparable analysis with this disorder. Despite the likely imprecision of its estimates of risk, the family history method can be appropriately used to compare differences in risk between groups of relatives. Further studies using the family study method, however, will be required to address more definitively the hypotheses investigated here.

Finally, compared to the probands with restrictive other personality disorders, a slightly larger proportion of the borderline probands were assessed with the help of two informants rather than one. Although this difference was not statistically significant, it may nevertheless have led to differential opportunities for identifying disorders between groups. However, the greater risks were only observed for the affective and impulsive personality disorder traits and not for other disorders presumably subject to the same bias. Furthermore, the proportion of schizophrenic probands for whom there were two informants was substantially larger than the proportion for borderline personality disorder probands, perhaps because this illness leads to greater family involvement and cooperation. However, the risks for affective and impulsive personality disorder traits, and only these traits, were similarly greater among the relatives of the borderline personality disorder probands when contrasted with the relatives of this secondary comparison group. Thus, the results obtained do not appear to be readily attributable to differences in the number of informants among proband groups.

CONCLUSIONS

The borderline personality disorder diagnosis is applied to individuals with several maladaptive traits, in particular, affective instability and impulsivity. Although the family history method has inherent methodological weaknesses and can thus rarely resolve questions of familial transmission, a familial, and possibly genetic, factor associated with these traits is suggested by the observed greater risk for both kinds of traits among the relatives of the borderline probands. In the light of these data and recent evidence for associations between biologic factors and behavioral dimensions (11, 24, 25), the evaluation of the dimensional approach to personality disorder traits, as well as categorical approaches using the more comprehensive and accurate family study method, may further clarify possible genetic/familial factors associated with borderline personality disorder.

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APPENDIX 1. Criteria for Affective and Impulsive Personality Disorder Traits

Criteria for Affective Personality Disorder Traits

Both A and B are required:

A. Patient has a lifelong and current mood disturbance characterized by one or more of the following: 1) depression or another dysphoric mood (e.g., anxious, irritable, worried), 2) expansiveness, 3) moodiness, 4) fluctuating mood swings. This disturbance is not accompanied by 1) chronic highly severe mood disturbance, 2) psychomotor agitation or retardation, 3) psychotic features, 4) extreme guilt.

B. At least one of the following is chronically present: 1) easy disappointment or self-pity, 2) low self-esteem, 3) lack of satisfactory intimate relationships, 4) pessimistic attitude.

Criteria for Impulsive Personality Disorder Traits

Both A and B are required:

A. At least three of the following are chronically present: 1) physical fighting with others, not associated with alcohol, 2) unpremeditated stealing (e.g., shoplifting), 3) problem with drinking or drugs, 4) binge eating, 5) problem with gambling, 6) promiscuity, 7) self-damaging acts (e.g., wrist slashing, head banging, frequent damaging accidents), 8) irrational angry outbursts, not associated with alcohol, 9) overreaction to minor events, not associated with alcohol.

B. Patient does not meet criteria for chronic schizophrenia, schizoaffective disorder, or antisocial personality disorder.

Psychiatry in Eastern Europe Today: Mental Health Status, Policies, and Practices

Jochen Neumann, M.D.

The author describes the impact of the recent social and political changes in Eastern Europe on psychiatrists and psychiatry. The observations contained in this paper are drawn from his personal experiences as a practicing psychiatrist in East Germany who also served as a member of the Executive Committee of the World Psychiatric Association from 1984 to 1989. The practice of psychiatry in Eastern Europe before the recent social and political changes was highly variable depending on the country, the locale of practice, and the social and political positions of the involved psychiatrists. Adapting to the recent changes will be very difficult, and it will be a long time before the modernization of psychiatric practice in Eastern Europe takes place. Psychiatrists in the Western world can play an important part in the future development of psychiatry in Eastern Europe. Their understanding of the current situation and the historical forces that shaped it is extremely important to the psychiatrists of Eastern Europe.
(Am J Psychiatry 1991; 148:1386-1389)

Eastern Europe is currently undergoing profound changes. These changes affect each stratum of social life and the destinies of all individuals. The psychological and social consequences are significant. To someone not living in one of these countries, they may be hard to understand.

In the eyes of the international public, the failure of Communism in Eastern Europe is mainly due to an economic disaster. This, however, is only one part of it. The protests and revolts of the citizens of these countries, whose needs in terms of consumption and comfort are very modest, were at first not aimed against economic living conditions. Rather, it was the psychological

conditions of public life (e.g., total surveillance; spoon-feeding; absence of a right to a say; restrictions of all kinds; lack of freedom of thought, culture, and religion; and special rights for privileged groups) that had become unbearable. It is my opinion that Communism in Eastern Europe has failed mainly because the deteriorating psychosocial conditions pushed the majority of the population into a state of social, psychological, and, in many cases, somatic disorder approaching disease as defined in the latest modification of the World Health Organization (ICD-9). This refers not only to the manifestation, severity, and duration of classical psychiatric diseases, which are more or less subject to the environment, but also to the quality of psychological health.

The more complex the structure of a society the more difficult it is to cope with it. A state of confusion and incomprehensibility, abstractness of social structures combined with a lack of control options, and helplessness resulting from feeling at the mercy of the society's compulsive mechanisms, rather than absolute hardship of living conditions, leads to psychological disorder. These conditions have been typical of all Communist countries in Eastern Europe during recent years.

In democratic countries and structures, the feelings,

Presented in part in a brochure published in Milan, Italy, to honor Professor Carlo Cazullo. Received Oct. 29, 1990; revision received Feb. 28, 1991; accepted March 18, 1991. Dr. Neumann is Ärztlicher Direktor of the Bezirksfachkrankenhaus für Neurologies and Psychiatrie Ueckermünde in Ueckermünde, Germany, and past Vice-President of the World Psychiatric Association. Requests for reprints may be sent to Dr. Neumann at Ravensteinstrasse 23, 2120 Ueckermünde, Germany, or to Allan Beigel, M.D., The University of Arizona, Administration Bldg. 702, Tucson, AZ 85721.

The author expresses his deep appreciation to Dr. Allan Beigel for his editorial help and guidance in the preparation of this paper.

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demands, and expectations of the citizens result in their participation in the shaping of the environment and in the delegation of both responsibility and power. In Eastern Europe, citizens often experienced reprimands and regimentation of their feelings, demands, and expectations. The outcome was an uncontrolled abuse of power and, in the end, resignation, repression, and aggression. Whole nations or nationalities gradually got psychologically disordered or sick.

Seen from a psychiatric or psychological viewpoint, the present period of *Perestroika* is no less traumatizing than the past. As a matter of fact, we are in what could be called a state of primal chaos—catastrophe and opportunity at the same time. The situation we are facing in the Eastern bloc can well be compared with the 1789 French Revolution, even if there is no guillotine. Power vacuums lead to legal uncertainty that can approach lawlessness. Many laws are declared invalid or ineffective; new ones have not yet been made or legitimized. Everybody is suspicious, and everyone suspects. Added to the economic crisis are the moral, judicial, philosophical, and cultural crises. Values that were binding and predictable in the past are gone without the establishment of new equivalents. In most countries, there is a lack of objects of identification. Fear of poverty and unemployment weigh heavily on many people. The “biologically” stronger often dominate the weaker, and unscrupulous profiteers abuse this time of transition for their own benefit. Learning democracy is almost as painful as living under dictatorship. Anarchic moments cannot be ignored. The old apparatus has been deprived of its power, and the new social forces still lack experience.

Despite Western concerns, institutionalized political abuse of psychiatry has not been a major factor in all Communist countries. Nevertheless, psychologically sound but undesirable persons who were presumed to be political enemies were discriminated against with the support of psychiatry, at least in one well-known country. These individuals were observed and kept in special hospitals and isolated from the public.

Developments have advanced so unexpectedly fast that new legislative and executive structures have not had time to emerge and become established. Not all of the priorities have been set. Many people are virtually uprooted. Many old, convinced, honest, and loyal Communists and sympathizers find themselves, all of a sudden, in a state of personal and political anomie.

Moreover, disagreement and fragmentation rule the new and ever-growing leadership groups. In many countries, it is only the churches that maintain their influence over society. Emotions have taken the lead, especially in Germany, where two states that once represented two socially antagonistic systems have to grow together again. It is extremely difficult, from a psychological point of view, to make all people understand that democracy, too, is somehow linked with order and integration.

Also, almost no one in Eastern Europe is prepared to cope with the living conditions of Western Europe. The old regimes have spoon-fed and patronized the people,

not allowing them to take part in decision making or to assume responsibility.

No matter whether you were lazy or diligent, you did not face a social risk. Now people are suddenly and unexpectedly subject to competition and the pressure to do well. Many people have to find a new identity. It will take years until identity, dignity, pleasure, and social security return for the majority of the population.

It will only be step by step, and probably not before the next generation, that people will learn to make use of their new freedoms and options and find a creative approach to democracy. On the way to this objective, the health system and the psychiatrist will bear an extraordinary responsibility for the psychological well-being of the citizens, for the promotion of a comprehensive mental health policy, and for the advancement of clinical psychiatry.

HEALTH, MENTAL HEALTH, AND SOCIAL SERVICES POLICIES

Although there were some quantitative differences, health and social services systems in the Eastern bloc were basically governed by the apparatus of the Communist Party. The supposedly competent state-run institutions (private and some church-owned facilities were irrelevant), ranging from those operated by the ministries down to those operated by local community authorities, were nothing but executors of a centralized policy based on quasi-feudalist principles. Health and social policies did not have their own independent stature in Eastern Europe during the post-World-War-II period. As has been the case in other spheres of social relevance, things could be put into practice only when ordered by the central authorities. This is not to ignore the fact that there were some competent individuals at all levels of the state and the party who, being aware of the problems prevailing in these countries and supportive of the ideals they found in more industrialized Western states, did everything they could within their sphere of responsibility to prevent the worst. With an utmost degree of diplomacy and a certain conformism that was simply unavoidable for survival, they tried to close the distance between policy-determined standards and more modern Western standards and to prevent injustice and local catastrophes.

In spite of the efforts of a great many colleagues over the last several decades in the panels of state and party management, in the local and central medical and scientific societies, and in individual institutes and clinics, they were not able to create a systematic mental health policy that would cover an entire country. They accomplished a lot in a pragmatic way to help the psychologically disordered and to prevent psychological disorders, and they often did so with the protection or at least tacit connivance of party functionaries at various levels. This should not be ignored.

It is also important to note that a mental health policy satisfying modern needs could not have been worked

out for the simple reason that the basic data necessary for this purpose were not available. Many interrelations critical to policy formulation could only be guessed at by using indirect means, such as the number of alcoholics and the suicide and crime rates. As a whole, whatever health and social policies that did exist were aimed at preventing local and national catastrophes, at concealing the true state of health of the population, and at avoiding any political complications or scandals, especially in foreign politics.

In this context, attention should be drawn to the fact that in almost all countries of Eastern Europe a one-sided picture of man had been officially propagated for decades. The picture drawn is that man is basically good and does not make mistakes. He lives in a Communist society that strives for the best for all human beings. There is neither human aggressiveness nor weakness and guilt, and there is no room for social conflicts, at least not at the level of society as a whole. Equating society and the state in the end caused the decay of society. Existing problems were hushed up, negated, or branded as the heritage of capitalism. The psychosocial framework was complicated by a whole variety of other factors, such as state-ordered atheism, prohibition of conscientious objection to military service, one-sided cultural policy, and an authoritarian approach in all spheres of social life, especially in the national education system and in the administration of justice.

The vast majority of the citizens, exclusive of bureaucrats and functionaries, were forced to live with a sociologically split ego. The decency, dignity, discipline, and order that were demonstrated to the outside were in stark contrast to the accumulated inner emotions, fears, worries, pain, and even anger and hatred. These conflicts often led to aggressive and destructive behavior as well as a lack of security, love, and the unrestricted right to exist.

The sensitivity of the new political forces in Eastern Europe to improved psychological and social aspects of human existence is great. Most recognize that there are models and experience, mainly in the countries of Western Europe and North America, which can be adapted or at least partially taken over. It is important for the Western world to recognize, however, that we need support to set up our own concepts that correspond to the history, world outlook, tradition, and culture of the relevant target groups in our countries. The omnipresent economic, political, judicial, and moral chaos, along with a still unclear future and the tumult of contradictory feelings among diverse and nonhomogeneous groups, requires concepts and steps that can be worked out and put into practice only in the countries or nationalities themselves and by the citizens of those countries in their native tongues.

THE PSYCHIATRIC SCENE

Academic programs and courses in medical education, with certain differences among the individual countries,

have struggled for years to approach a modern international standard. At some sites, emphasis is on practical skills; others focus on theory. There are schools that emphasize the biological aspects of psychiatry; others give priority to social and psychological aspects.

Within the last 20 years, travel restrictions and lack of hard cash have made education even more difficult because of a lack of international communication and a beginning information deficit. Only a few institutions are still capable of imparting practical experience regarding the application of modern pharmacotherapeutics, and only a few have state-of-the-art medical equipment and data processing systems.

Postgraduate training mainly takes place in the hospitals. Its quality corresponds to the quality of clinical care. Many countries have central academies for medical in-service training where doctors attend short courses. The level of this in-service training is generally equal to that of the universities. Its efficiency, however, is usually limited by the short period of time of such training. These academies publish their own manuals and journals.

With very few exceptions, the national journals in the Eastern bloc do not meet international standards in terms of printing quality or content. Because of import restrictions, only elite institutions receive specialty journals from abroad. National professional societies and, through them, the World Psychiatric Association, are virtually the only window to the outside scientific world.

Original research hardly exists any more in Eastern European countries and, if present, occurs only on a joint basis with Western clinics, institutes, and firms or thanks to close personal ties between individual scientists. The largest part of this scientific work involves coauthorships for specific subjects and projects that have been scheduled and set up abroad (mostly in Western Europe, North America, and East Asia). Usually they relate to application research, that is, a scientifically based adaptation of already existing knowledge to the concrete conditions of Eastern Europe.

Self-isolation, information deficits, and poor command of foreign languages also have had a negative impact on the situation. Younger colleagues who have no friends and contacts abroad now tend toward resignation, poor motivation, and a certain lack of interest, especially given the fact that scientific success was rarely honored in the past. A mediocre scientist could have a good career if he or she was on good terms with the party and state bureaucracy, but serious work and proficient results often did not result in success for one who was not in good standing with the bureaucracy.

In the countries of Eastern Europe, there have been only a few truly creative and original scientists and thinkers in the field of psychiatry, but those few are still there. Almost all of them have had to pay for their chance to do scientific work by giving up their independent world outlook and political autonomy and adopting a formal conformism with the system. A few may have even violated ethical standards, in part out of conviction or because they were abused. No one could

carry out creative functions for a long period of time without formally agreeing with the ruling system and being willing to do so publicly. These extreme bureaucratic burdens frustrated most original thinkers and research scientists. As a result, even proficient and diligent scientists in Eastern Europe will lag behind their colleagues in the West for many years to come.

In the majority of Eastern European countries, teaching, student training, and research in the field of psychiatry have been combined with other disciplines at the universities, academic clinics, and institutes. Pure psychiatric training sites and research institutes are rare. Industry does not play any relevant role in psychiatric research.

The availability of inpatient and outpatient clinical psychiatric care differs to an unbelievable extent among the countries of Eastern Europe. The standards range from ultramodern clinics and outpatient departments to hospitals and health centers with an unbearable medieval milieu and a professional level that is at least two decades behind up-to-date Western standards. Without question, in many places the commitment, level of education, and proficiency of many colleagues have dropped.

Eastern European countries do not have a mental health policy, a realistic price-performance structure, an acceptable performance-wage relationship, an adequate state of repair of their buildings, available medicine, therapeutic approaches, appropriate equipment, or adequately trained physicians, psychologists, nurses, and social workers. Further, available resources have not been allocated equitably. Large cities, especially the capitals, have priority over the smaller towns and rural communities, acclaimed clinics over unknown ones, personally established directors over unknown executives, privileged target groups over the man in the street.

As a result of these conditions, psychiatrists are concerned and affected in many ways in both their private lives and their professional situation. Today, most of our colleagues may be viewed as belonging to one of two large groups: 1) a very large group of older, competent, and experienced psychiatrists who have a share in bearing the responsibility for the past through their conformism, adaptation, weakness, or, and this should not be forgotten, their conviction and 2) a smaller group of mostly younger, not so experienced or proficient colleagues who are still free of joint guilt and entanglement with the past. In addition to these two large groups, there are two smaller groups: 1) a group of steadfast and convinced fighters of injustice who, because of their opposing position to the ruling bureaucratic system, have for the most part not been able to distinguish themselves in their profession, and 2) an even smaller group who, either as a result of abuse or from conviction, used to be the tools of the old regimes and clearly violated laws and ethical standards of the medical profession and/or materially profited from the situation.

The steadfast fighters are now being vindicated and promoted, and the guilty are being punished. It is the members of the two large groups who have to push ahead with the development of a mental health policy

that establishes psychiatry as a well-accepted clinical and scientific-medical discipline. The younger generation will grow into this new time and its tasks, working out the necessary convictions and ideals as they acquire knowledge and proficiencies, with the help of support from abroad.

The older generation is of special significance for the present and for the near-term future because of their professionalism, knowledge, and capabilities. They should also receive support, but with a minimum of trust. The amount of this trust should be linked to supervision, in much the same way as former alcoholics would be managed—praise for their successes as long as their attention to sobriety prevents them from drinking again.

THE NEAR-TERM FUTURE

It is highly unlikely that the existing deficit in strategies, concepts, experience, and care relating to psychological health and psychological disorder can be compensated for without help from the outside, at least in a period of time acceptable to the citizens, patients, and professions involved. The same is true for the financial and technical preconditions. As I see it, outside technical and financial support is desirable, given the fact that the economic situation in all countries is a disaster. Moreover, there are neither plans nor production capacities for state-of-the-art medical equipment, data processing, and pharmaceuticals. On the other hand, capacities for the design and the construction of buildings can be worked out rapidly. What matters even more are educational and training programs and material for as many colleagues as possible, better access to specialist literature, and more conferences and congresses with a greater involvement of Eastern European colleagues. Existing strategies and models for a mental health policy should be checked for their convertibility and adaptability to individual Eastern European countries.

It would be desirable if colleagues from advanced countries could understand the extremely embarrassing psychological situation of their colleagues in Eastern Europe. Inhibitions due to long years of communication deficits, language barriers, feelings of being forced to ask for help like a beggar, the awareness of professional incompetence and of political coresponsibility or guilt for what happened in the past, loss of moral values, the search for new objects of identification, a major lack in orientation, and feelings of helplessness place a heavy burden on psychiatrists' shoulders. What psychiatrists in Eastern European countries need from their Western colleagues most of all, therefore, before any education and training and even before any financial and technical help, is moral support and integration into the all-embracing world family of psychiatrists. Some of the large and intellectually powerful national psychiatric societies could do wonders for both psychiatric patients and their colleagues in Eastern Europe by reaching out. We would welcome it.

Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

PSYCHODYNAMIC PSYCHIATRY

Psychodynamic Psychiatry: Theory and Practice, vol. I, by John Frosch, M.D. Madison, Conn., International Universities Press, 1990, 359 pp., \$50.00.

Psychodynamic Psychiatry: Theory and Practice, vol. II, by John Frosch, M.D. Madison, Conn., International Universities Press, 1990, 503 pp., \$60.00.

John Frosch is one of America's great psychiatrists. He was the first editor of the *Journal of the American Psychoanalytic Association*. He has read many psychoanalytic and psychiatric papers and has seen many patients. His long years of experience and the theoretical and clinical knowledge gathered during that time come forth in this two-volume work that preserves what is of value in the old while incorporating what is essential in the new. What is rare about these volumes is the fact that they contain so much but read so easily. Inevitably, a textbook by one author leads to areas where we would like more depth, but the comprehensive view Dr. Frosch provides makes up for these thin spots. Dr. Frosch writes about psychodynamic psychiatry as he sees it and uses it to treat a vast variety of patients.

The two volumes comprise three parts. In the first, the introduction, Dr. Frosch discusses the need for a psychodynamic approach to psychiatric entities. In the second, he sets forth general psychodynamic principles, and in the third he applies these principles to the traditional clinical categories.

Dr. Frosch is a conservative Freudian who views drive psychology as having precedence over object relations. The ideas of Bowlby, Kernberg, Kohut, Winnicott, and even Melanie Klein find their way into the text, however, and not just to be summarily dismissed. In fact, Dr. Frosch explicitly states that the separation of anxieties arising from psychosexual phases and those arising from object relations is completely artificial.

In addition to not being doctrinaire about psychoanalytic theory, Dr. Frosch is open to a wide variety of biological contributions to psychiatric illness. There are many other authors, however, who will keep us informed about these areas. There are very few John Frosches left to translate *DSM-III-R* for the overly busy resident, reveal how symptoms have meaning, and instruct us as to how nearly a century of psychoanalytic thinking aides us in understanding the mind of a psychiatric patient no matter what the diagnosis.

This text is enriched with such gems as three of Freud's letters of consolation in the section on mourning, Henry James's discussion of the impact of physical illness on one's emotional life, and Dr. Frosch's own interview with a schizophrenic patient who uses one word to mean many things. On the negative side, it is inconvenient to have all references listed at the end of volume II. One has to keep volume II at hand while reading volume I to find where a cited publication can be found.

Dr. Frosch is traditional enough to continue to refer to char-

acter disorder rather than personality disorder and to retain manic-depression rather than bipolar disorder, all of which fits with an emphasis on the older literature. Students, residents, and younger psychiatrists need a place to find old wine in new bottles, providing that it is from a very good year and still at its peak. Dr. Frosch has selected from the best. Toward the end of a long, broad, and deep career, John Frosch is at his peak, and this book is evidence.

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CHILD PSYCHIATRY

The Course of Life, revised ed., vol. II: Early Childhood, edited by Stanley I. Greenspan, M.D., and George H. Pollock, M.D., Ph.D. Madison, Conn., International Universities Press, 1990, 478 pp., \$50.00.

This book will be valuable for all psychoanalysts, all child and many adult psychiatrists, and anyone seriously interested in human growth and development. It is a revised, expanded, and updated version of a 1980 volume from the same distinguished editors, as part of their continuing landmark series, *The Course of Life*. Originally, volume I covered both infancy and early childhood. In the current edition, volume I concerns infancy and volume II, under review here, concerns early childhood, centering on ages 1 through 3. About half of the chapters are new or substantially revised.

The collection is predominantly but not totally psychoanalytic and contains complex up-to-date major papers by famous clinicians and theoreticians. It is something of an establishment book. In my opinion, however, it is more a loss to accuracy than a gain that this volume drops the previous volume's fair subheading: "Psychoanalytic Contributions Toward Understanding Personality Development."

Studies of human biopsychosocial growth and development have gained in data, theory, and integration in recent years, probably especially in the realm of the first few years of life. The current book somewhat displaces a previous generation's central focus on Freudian psychosexual orality and anality and Eriksonian psychosocial trust, autonomy, and initiative. It centers much interest on separation-individuation and adds useful attention to temperament, aggression as a complex developmental area, clinical assessment, and a bit about day care. I would suggest that a chapter on language development, and perhaps one on other than maternal child care, might have been worth adding.

The current book is not an integrated presentation of a single point of view. There are valuable and unique things in each chapter, but there is also considerable overlap and some redundancy, with many partial agreements and partial disagreements among the various authors, especially in their more general theoretical psychoanalytic positions and discussions.

There are also some instances of firm insistence on a theoretical point not widely accepted as worthy of such insistence. Appreciating the many agreements, what are we to do with the disagreement? How do we resolve them? One is reminded of some basic problems of psychoanalysis, explored, for example, by Grünbaum (1), and reminded that data from fields beyond pure psychoanalysis have often usefully been called in—here and elsewhere—to clarify and solidify psychoanalytic theory.

Sally Provence, who has long embodied excellence in combining analytic theory with direct observation of infants, contributes a chapter on "Direct Observation and Psychoanalytic Development Psychology: The Child From One to Three." Margaret Mahler and John McDewitt contribute two authoritative chapters on separation-individuation, identity formation, object constancy, individuality, and internalization, and Erna Furman adds a chapter on "Mothers, Toddlers, and Care."

Three chapters are by Henri Parens, two of them on aggression. Parens recapitulates and then reformulates the psychoanalytic history of aggression, in the process considering some evidence and theory for separating assertion from destructiveness and restoring aggression to a central position in developmental theory. He tries to establish and describe developmental stages and events in infant and toddler aggression, an "epigenesis of aggression," emphasizing—a major and productive position—that "aggression *develops*."

Stella Chess and Alexander Thomas contribute a clear essay on temperament; in contrast to other chapters, it includes much attention to what data were collected and how as well as what categories were developed. They consider temperament a useful mediating variable between environmental stimuli and demands and patterns of neurobiological organization. They also explain their concept of "goodness of fit" as a useful model in tracing behavior disorders, for treatment and prevention, and for healthy self-esteem.

Marian Tolpin and Heinz Kohut contribute "The Disorders of the Self: The Psychopathology of the First Years of Life." Their chapter is, in several senses, self-centered, and it seems to me to assert a child theory based on adult theory with relatively little direct or clear evidence from children 1 to 4 years old.

Eleanor Galenson's chapter on psychological development during the second and third years touches on oral, anal, genital, ego, and language development, as does Parens' longer third chapter, on the second and third years, which contains comparisons and a useful table on developmental frames of reference. Albert Solnit, one of the fathers of the field represented by this book, more briefly provides an overview of ages 1 to 3 and gives useful clinical case examples. Calvin Settlage adds a further good overview of the second and third years of life.

Stanley Greenspan and Alicia Lieberman apply a "developmental structuralist" approach, taking into account both psychoanalytic and Piagetian developmental psychologies and trying to develop instruments of quantitative clinical assessment for ages 18 to 36 months in which cognitive and emotional factors are simultaneously examined. They give case examples and provide a several-page scale of measures of representational play. Peter Neubauer, in the final chapter, briefly presents "Phase Specific Disorders of the Second and Third Years of Life," subdivided into libidinal, ego, and object relations disorders.

Overall, this is a complex and useful up-to-date collection

of essays by major figures in and around the field of psychodynamic development in early childhood.

REFERENCE

1. Grünbaum A: *The Foundations of Psychoanalysis: A Philosophical Critique*. Berkeley, University of California Press, 1984

LAWRENCE HARTMANN, M.D.
Cambridge, Mass.

Behavior Problems in Preschool Children: Clinical and Developmental Issues, by Susan B. Campbell. New York, Guilford Press, 1990, 270 pp., \$30.00.

The title of this book at first glance would lead the reader to an oversimplified expectation of the contents. In the first section, however, the author states, "Although several theorists have attempted to account for either cognitive development (e.g., Piaget) or psychosexual development (e.g., Freud) with comprehensive theories, large scale theories have played a relatively small role recently in the field of child development." The first chapter deals with theoretical issues such as the transitional model, ecological models, and temperament. Chapter two is devoted to developmental issues such as cognitive and social-cognitive development, pretend play, separation-individuation, and the development of a sense of self as well as the development of language and memory. Chapter three is devoted to clinical issues such as how one can separate annoying behavior from a real problem and provides four individual case histories that are referred to throughout the volume.

Chapter four addresses family factors, and chapter five deals with sibling relationships. Chapter six concerns itself with peer relationships and chapter seven with treatment approaches. Chapter eight presents follow-up and outcome, and chapter nine is entitled "Conclusions and Social Policy Implications."

The author does a creditable job of reviewing the literature. Unfortunately, it is not often easy to determine which are worthwhile articles and which are not. Another inescapable fact is that many of the studies indicate only that "most youngsters" or "more youngsters" are affected by certain factors. One may be left wondering what "most" or "more" really mean and whether exceptions are numerous or few.

Not infrequently, "findings" are presented as if they were new, when in fact they may be things we have always known. For example, "Problem children and older siblings were less likely to become engaged in constant battles or at least battles that were serious enough to come to the attention of the parents." Certainly, most smaller younger brothers soon learn that picking a fight with an older and stronger brother is not particularly wise. Similarly, they point out that intuitive parents recognize that the older sibling requires additional attention when the next younger one is born. They realize that if this is not done the older child will literally feel left out in the cold. Perhaps the reason for such statements is that there are parents who are unintuitive and who need help in recognizing these factors.

Probably the biggest reasons a book of this broad scope has not been written are the number and type of variables that need attention, the awareness that unpredictable changes are constantly occurring, and the fact that it is impossible to measure accurately some of these variables.

We do know several things that promote mental and emo-

tional health in youngsters as well as several others that delay and distort it. We are aware, for instance, that two mature adults who love each other and want to have a family represent a good start. They are intuitive about children's needs at different stages, agree with each other, and share responsibilities. They plan and try to time the spacing of their offspring. If one looks at our own society today one does not often see such a family. We have far too many divorces and too many unwanted pregnancies among teenagers who are ill equipped emotionally to accept the parental role. Probably the most important role in our lives is that of a parent, but we usually have to learn it from our own parents, who often fall short. Children, fortunately, are quite resilient, but they can take only so much. Parenting classes are of some use, but, as the author points out, they do not solve the whole problem. The basic question would seem to be, Is having children a right to be given to anyone under any circumstances or a privilege for those who have attained the capacity to be an adequate parent? The answer is complex, but certainly if infants and preschoolers were magically given a vote there would be little doubt how it would turn out.

The author raises another philosophical problem. In years past children were the property of their parents to do with as they wished. This proved disastrous. The author leans toward more government rules and regulations, but is this goal enforceable? It should be remembered that the notion that the child "will grow out of it" is dangerous. The child should be watched over time. This book is quite readable and belongs in the libraries of both professionals and nonprofessionals.

STUART M. FINCH, M.D.
Tucson, Ariz.

The Significance of Infant Observational Research for Clinical Work With Children, Adolescents, and Adults, edited by Scott Dowling, M.D., and Arnold Rothstein, M.D. Madison, Conn., International Universities Press, 1989, 257 pp., \$32.50.

In 1976 the Program Committee of the American Psychoanalytic Association began a series of workshops for mental health professionals in an attempt to demonstrate to mental health clinicians the usefulness of psychoanalytic thinking. The workshop led to the publication of an annual monograph. *The Significance of Infant Observational Research for Clinical Work With Children, Adolescents, and Adults* is the fifth in this series and reflects the current interest in infant research. The monograph includes clinical presentations by child and adult analysts who come from different theoretical and clinical persuasions. These authors share with the reader their perspectives on how data from infant and child research have affected their theoretical constructs and clinical work with patients of differing ages, sexes, and diagnoses. After the presentation of clinical vignettes the work of each of the primary contributors is critiqued by four discussants and followed by a summary epilogue. Despite their differing perspectives on the usefulness of infant observation and infant research, all of the authors agree that such knowledge is broadening and may be useful clinically in understanding patients. They disagree on the degree of usefulness of such observation to the therapeutic, analytic process. Some authors suggest that observation of the infant only allows for data to be accumulated about the behavior of the infant and gives no insight into the development of mentation, cognition, and reality. Other authors

note the danger of predicting future development of psychological health or pathology from observations of the infant. They note that development is not necessarily continuous but may, in fact, be discontinuous and that even a child subjected to intense trauma may be invulnerable.

Finally, some authors caution that psychoanalytic theory should not follow automatically from infant observation. Theory must first be constructed and then fine-tuned from observational data (the newest infant data have been gathered by exotic and complex technologies). The new data do not necessarily confirm or invalidate old theory (such as structural theory or object relations theory), nor do they allow for a completed new and different theory. However, at this time, they do supplement existing theory by using "the electronic revolution," which allows for detailed, direct observations of the most minute changes in an infant. A researcher today has a new source of data—not adult recollections of childhood or data from child analysis but, rather, detailed and direct observation of infants. It would be interesting to follow some of the infants longitudinally and see if predictions made about development came to fruition.

This monograph certainly contributes to the general reader's knowledge of current analytic thinking about the significance of infant observational work and allows the general reader to keep abreast of the contributions from the field of psychoanalysis. Unfortunately, material such as presented in this monograph would be more lively, stimulating, and exciting if one were attending a meeting. Important scholarly material can become too dry and too difficult to absorb when presented for the first time in essay form. Thus, this book, although it elucidates current thinking and provides essays by talented and well-respected analysts, is not always as stimulating as a panel or symposium on the same subject. It does, however, offer an inside view of what analysts today believe is the significance of current infant research and an opportunity to read about technical advances and how such research may be integrated into clinical practice.

ELISSA P. BENEDEK, M.D.
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Straight and Devious Pathways From Childhood to Adulthood, edited by Lee N. Robins and Michael Rutter. New York, Cambridge University Press, 1990, 379 pp., \$59.50.

Recent epidemiologic studies conducted in the United States, Canada, Puerto Rico, and elsewhere show that many adults with major psychiatric disorders retrospectively report that the first onset of these disorders was in adolescence or childhood. This still does not tell us the prognosis for a child with a psychiatric illness or whether the childhood forms of depression and anxiety are the same as the adult disorders. As the authors in this impressive volume note, childhood personality and behavior forecast adult problems in adult life, yet many children with severe problems turn into competent adults. There is reason to believe that disorders such as depression may be different in their childhood and adult forms. Take, for example, the case of antidepressant medication. The efficacy of such medication for depressed adults has been well established through controlled clinical trials. The few similarly designed trials with depressed children have yet to show a strong effect, suggesting that depression in childhood and adulthood may differ.

Robins and Rutter, the giants of long-term studies of chil-

dren, have joined together to glean the latest findings on the pathways from child to adult psychiatric and behavioral disorders. Having the celebrities of the field edit a volume has several advantages. The most obvious is that they have been able to select from among the best work from leading authorities (e.g., Gould and Shaffer on suicide, Tienari and Wynne on adoption studies of subjects with schizophrenia, Chess and Thomas on continuities and discontinuities in temperament, and Kendler and Cohen on personality and behavioral problems).

Moreover, the authors show that their celebrity status is well earned. They are methodologically sophisticated and well aware of the pitfalls of longitudinal studies of children, namely, that the children, the investigators, and/or the funding may disappear over long periods of time. Perhaps more importantly, they are not ideologically bound to any one concept of etiology. Well represented in this book are investigators with credentials in genetics (e.g., Erlenmeyer-Kimling and Mednick) as well as those who have a clear grounding in studies of psychological and psychosocial variables affecting outcome.

In selecting the papers, the editors have moved beyond nose counting, which is a limited use of epidemiologic studies, and have instead tried to find evidence for predictions of outcomes. Under what conditions do good and bad outcomes occur in children as they grow up? The book covers problems in follow-up studies due to death and the adult outcomes of childhood personality disorder, hyperactivity, parental absence, and institutionalization. The antecedents and consequences of substance abuse, particularly cocaine abuse; the continuities and discontinuities in temperament; and studies of children at risk for psychiatric disorders because they have parents with similar disorders are also covered. The chapter authors deal clearly with long-term follow-up studies, particularly the work of Quinton and Rutter on longitudinal studies of children.

This volume is full of statistics, tables, charts, and research results. It is a research monograph rather than a clinical essay and will be well appreciated by researchers. However, the findings have direct relevance to psychiatrists and mental health professionals in clinical practice.

Obviously, child psychiatrists need to know the latest on the course and outcome of childhood psychiatric and behavioral problems. However, there is increasing need for adult psychiatrists to be well grounded in the facts as well. The consumer movement and public education efforts by the National Institute of Mental Health have made the public aware of the signs, symptoms, and course of mental illness as well as the possible treatments. The familial nature of most psychiatric disorders has also been described. Increasingly, adult patients are concerned about the risks and potentials for similar illness in their children as well as the prognosis of early signs. The material contained in this volume should be reviewed by the practicing mental health clinician.

MYRNA M. WEISSMAN, PH.D.
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DSM-III-R Training Guide for Diagnosis of Childhood Disorders, 2nd ed., by Judith L. Rapoport, M.D., and Deborah R. Ismond, M.A. New York, Brunner/Mazel, 1989, 224 pp., \$27.50; \$17.95 (paper).

Children's behavior patterns are a source of both concern and bother to the world around them. Aberrant adult behavior

may prompt similar responses, but the child must rely on others to seek help. Children rarely knock on our doors or phone for appointments. Therefore, we need careful assessment of their problems and clarity in their diagnosis as well as a book to explicate our progress in making that clarity more real and understandable.

Were it not for the literary and scientific reputation of Dr. Rapoport, the promise of this book might be that of a school text to be held for reference but not read. That would be a mistake.

Child psychiatry, a delinquent in the medical research arena, has seen diagnosis evolve, as has the field of psychiatry itself. Dr. Rapoport, a leader in resolving the multiple approaches to a workable system, sets forth with Deborah Ismond both the current nosology and the rationale for it. It is the latter that makes this book more than a dusty text.

Taking into account both the wide range of forces impinging on the child and the equal range of the training and modalities of practitioners who serve the patient, the authors do a great deal to clarify the present picture of a diverse field of care. In doing so, they somewhat formally clarify the meaning of the axes to make them useful for clinical practice as well as research. The emphasis, reflecting the bent of the authors, is on research, but there are serious attempts to translate the overall nosology into clinical usefulness.

The book's review of the evolution of the field of child psychiatry brings out the core issues of the various schools of child care theory and practice (with a light touch and nod to the affective theories), the importance of multiple informants, the uses of psychological data, and the relation of the full diagnostic process to appropriate treatment.

Having established the conceptual basis of such a framework, the authors proceed, chapter-by-chapter, only to elucidate the easily defined disorders but also to discuss in readable detail the problems posed by the evolution of such concepts as the developmental disorders. The text brings order to issues of differential diagnosis compounded by growth, by intellect, and by the translation of adult terminology to the clinical pictures of childhood.

The knotty problems posed to clinical diagnosticians by autism, by the pervasive developmental disorders, and by the relation of these, if any, to childhood schizophrenia are thoroughly and understandably explored. So, too, are the areas of disruptive behavior disorders and the anxiety disorders, which have been the bread and butter of child psychiatric practice for most of the century.

The growth of diagnostic knowledge in the field of child psychiatry stumbles at times between the pressures posed by developmental concepts and by the more definitive symptoms of general (read adult) psychiatry. Thus, the chapter discussing mood disorders, matching the increase in diagnosed depression and suicidal behavior occurring earlier and earlier in the age spectrum, is most important.

The diverse practitioners in the area of child care often see children and their families from quite different points of view. There has always been a resistance on the part of these professionals (lately reinforced by groups related to patients and families) to put grave labels on children's behavior. Pediatric optimism and psychiatric pessimism often clash. Pathology, however, as this orderly compendium demonstrates, does exist.

Should one complain? I take issue with the authors' frequent use of the word "pediatric" as an adjective seeming to substitute for "child." Yet they pay scrupulous attention to other

areas, such as the involvement of parents and families in the diagnosis and, in so doing, call specifically for increasing attention to developing a more inclusive diagnostic formula.

Quite a satisfactory text and reference.

HENRY H. WORK, M.D.
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Psychiatric Disorders in Children and Adolescents, edited by Barry D. Garfinkel, M.D., F.R.C.P.(C.), Gabrielle A. Carlson, M.D., and Elizabeth B. Weller, M.D. Philadelphia, W.B. Saunders Co., 1990, 554 pp., \$47.00 (paper).

You teach child psychiatry to students and residents as a subspecialty of medicine rather than a subspecialty of social work. Then you have to provide the still missing, essential facts they must take with them to manage child psychiatry patients in their future practices. They challenge you to find a usable book.

Now you have an answer. *Psychiatric Disorders in Children and Adolescents* is the most pragmatic and comprehensive review of solid research in the field, organized for the working clinician but complete enough to start researchers on reviews of their topic. One sure marker of competence is that play therapy is briefly mentioned only once.

Unfortunately, some weaknesses are serious. Conduct disorder, the single most important childhood diagnosis, is the equivalent of and precursor to antisocial personality disorder. It has hard outcomes, including violent crime, youthful suicide, possibly AIDS, preventable accidents, substance abuse, child and spouse abuse, homelessness, and miscellaneous dependency states. The editors make their biggest error in selecting the chapter on this subject. It combines an apologist view of the character defects with obsolete, therapeutic nihilism. Most children with conduct disorders respond to tighter discipline or to anti-aggression drug regimens, missing from the book. It is true that neither approach has long-lasting effects. What treatment for any chronic condition remains effective once stopped?

The editors' lumping diagnoses into "internalizing" and "externalizing" groups has no clinical validity, only statistical support removed from reality. They tout the "biopsychosocial model," which I consider makeup on the corpse of the old psychiatry and a phrase that is too painful to pronounce ever again. An otherwise good chapter provides a 93-item scale to assess hyperactivity instead of the ubiquitous 10-item one. The authors fail to warn that giving stimulants to children with preclinical bipolar disorder presenting as hyperactivity will give parents a nasty surprise. Behavioral and medication protocols on dosing, on managing side effects, and nonresponders would increase the day-to-day utility of the book. Inpatient residents would appreciate a consistent way to sedate children for diagnostic procedures. The authors do not consider preexisting conditions as explanations for posttraumatic symptoms, nor do they suggest systematic desensitization for treatment.

When the data run out, the out-of-touch "professor" in the authors comes out: "Use of medication solely to control aggression and agitation [in retarded patients] can only be understood as a . . . chemical straightjacket." "No suicide attempter should ever be discharged directly from an emergency department."

The many case histories are useless. The publisher should save the paper and cut the excessive price in half. Clinicians,

students, and residents across the country would then find the second edition irresistible.

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ADOLESCENTS AND ADOLESCENCE

Psychotherapy With Adolescents, by Richard A. Gardner, M.D. Cresskill, N.J., *Creative Therapeutics*, 1988, 794 pp., \$35.00.

Few would doubt the potential value of this skilled clinician's account, based on a long and productive career, of his clinical observations and the knowledge he has drawn from them. With this in mind, I looked forward to reading and reviewing *Psychotherapy With Adolescents*. My hopes were dashed when I discovered that this long book, ranging over many related topics, is filled with strongly held beliefs about adolescence, social conditions, and psychotherapy. In fact, in the light of the vast terrain Gardner traverses, a more apt title for this narrative might be *My Reflections About the Nature of Adolescence and Society*. Ordinarily, I would be delighted to find an even richer book than I expected. Unfortunately, accompanying Gardner's breadth are his definitive opinions, pervasive biases, and simplifying views—often expressed as facts.

The author's views about individuals and society are seldom supported by any clinical, scholarly, or research evidence. Their basis is implicitly, and often explicitly, Gardner's "over 30 years of experience." When references are cited, they are most often to his own previous publications. I cannot possibly convey all of the complex issues that Gardner bypasses in his spirited personal reflections. Instead, in this review I will highlight his analyses of several major current topics, analyses that are especially troubling given the state of our knowledge and the dangers of prematurely choking off continuing open scientific discussion.

Adolescent development is discussed early in the book. Yet in no apparent way does the author acknowledge the numerous contributions from developmental psychologists who are systematically studying adolescent development (1–3). Moreover, there is a body of work that is highly relevant to the author's perspective on the evolution of conscience and his theory of the development of the capacity to experience guilt from modern psychoanalytic theory (4) and studies of moral development (5). Consistent with traditional wisdom about adolescent development, Gardner discusses the importance of autonomy and "rebellion" during this era of the life cycle. However, recent theoretical and empirical writings emphasize the important and, until now, neglected areas of adolescent relationship development, involving attachment and intimacy with one's family and the transforming ties with family members rather than the rupturing of these key bonds (3, 6).

Gender differences represent still another area into which Gardner boldly ventures. A rapidly burgeoning empirical and theoretical literature addresses many complex questions about the nature and basis of gender differences. Gardner, however, shows no recognition of this scholarship through explicit citation or modesty in his declarations as he points out gender differences in many chapters. For instance, in discussing internal guilt-evoking mechanisms, he asserts, "I believe that women are more likely to feel guilt on a genetic basis than men, and are more likely to put themselves in the position of

other people [and to] . . . exhibit sympathy and empathy" (p. 16). The rationale for this position is that "up until the 20th century men were primarily the hunters and fighters (protectors and warriors) and women primarily the child rearers" (p. 16). But even this "fact" is not documented. There is certainly much discussion these days as to whether women are more sensitive than men to relationship issues as well as speculation about whether this sex difference in affiliation is rooted in differential socialization (7, 8). There is no reference to this body of work. Furthermore, comments like "women are the quality controllers" (p. 63), "men . . . have been programmed to be promiscuous" (p. 64), and "I want mothers to be in the home more than fathers during the infancy period" (p. 97) are offered without acknowledgment of individual differences among men and women and without apparent scientific basis.

Society and education are also addressed throughout the book. In terms of society, Gardner, in several contexts, points out that Western society has become increasingly "psychopathic in the last 20–25 years" and that we are living in a "much more exploitative world" (p. 94). He draws many implications from these bold generalizations, including a justification for requiring parents' immediate payment of fees following each of his sessions with their child or adolescent. Turning to the topic of mass media, Gardner maintains that there is "little question that television and movies contribute to the development of various forms of psychopathology" (p. 103).

With respect to education, he says, "Those who are unfortunate enough to be provided with inadequate educational programs are likely to develop psychopathology" (p. 99). Beyond the high school level, Gardner notes that most (at least 80%) of educational programs are actually "winter camps," businesses designed to profit their "owners," without regard to the welfare of the "consumers," the students.

I have not done justice to the author's positions on a number of other major topics, including psychoanalysis, homosexuality, and the future of psychodynamic psychotherapy. He is consistent in his certainty surrounding these topics and in his use of numerous stereotypes—the "classical psychoanalyst," the "obligated homosexual." Diversity—among psychoanalysts, homosexuals, schools, and families—cannot be seen in these views. The author frequently refers to himself as outspoken. Being outspoken does not entail insensitivity to complexity or insisting on unwarranted clarity. In later chapters, Gardner presents his various therapeutic interventions and inventions (e.g., the "talking, feeling and doing game"). Regrettably, the cumulative effect of the preceding chapters, with their distracting simplifications and frequent unjustified conclusions, seriously interferes with the reader's ability to appreciate Gardner's more practical advice, culled from his many years of experience.

Psychotherapy With Adolescents is a troubling book, one in which the author gets in his own way through his unscholarly assumptions and theories about fundamental social and psychological questions. I cannot recommend this problematic book to clinicians, researchers, or scholars who are working in the important and complex domain of adolescence.

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The Teenage World: Adolescents' Self-Image in Ten Countries, by Daniel Offer, Eric Ostrov, Kenneth I. Howard, and Robert Atkinson. New York, Plenum, 1988, 270 pp., \$35.00.

Since 1962, Dr. Offer has challenged the "normality" of adolescent turmoil and urged theoreticians and clinicians to consider disturbance in adolescence more seriously (1, 2). The aim of this book is to demonstrate *universal* aspects of adolescent self-image, with data from 10 countries ranging from the United States to Bangladesh.

The first section introduces the study, which involved the administration of the Offer Self-Image Questionnaire to samples of high school students in each of the countries. The chapters that follow give a limited discussion of the literature on the self and the cross-cultural study of the self, discuss the research methodology, present results, and include an analysis of the findings. The "Commentary" at the end of the text by Harry C. Triandis is a valuable, if brief, critique. An extensive appendix includes the Offer Self-Image Questionnaire, its back-translations, and the results by country.

The cross-cultural study of the self is problematic, and the brief discussion of the theory and measurement of self-concept cannot do justice to this complicated phenomenon. The sophisticated work of Rosenberg (3) and Hauser (4) on child and adolescent self-concept is not noted. Similarly, only brief discussion is devoted to problems in the cross-cultural study of the self (5).

This study involved the administration of a translated and back-translated questionnaire to groups of secondary school students in several countries. The adolescents queried were literate, of at least middle-class economic status, and lived in urban areas. Such groups are not necessarily representative of adolescents the world over. For example, in Bangladesh, the literacy rate is 29% (6), and only 15% of the country's youths attend secondary school (p. 46). Similar rates apply to much of the Third and Fourth Worlds.

The analysis seeks to demonstrate that "universal adolescents" are "happy most of the time," "caring and oriented toward others," "value work and school," have "positive feelings toward their families," and "feel they can cope with life's vicissitudes." The authors conclude that "the results reported in this section were consistent with our expectations. Our data simply captured the *universality* of this experience" (p. 77; my italics).

Not addressed is the homogenizing influence of secondary education, delayed entrance into the work world, delayed marriage and childbearing, and the Westernizing forces of middle-class and upper-middle-class status (with its emphasis on consumer goods, mass communication, etc.) on identity formation, especially among teens. The authors assert that there is an emerging "global culture" resulting from widespread exposure to television and other media and from urbanization; the more interesting question of how these influences might interact with local cultures in shaping identity is not discussed. Nor do the authors deal with the great mass of teenagers in the world who are not in secondary school and who are not of privileged economic status.

The book is clearly written. As a first effort at studying adolescent identity cross nationally it is an important work that provides starting points for further research. As it stands, however, it offers little support of a truly universal adolescent "self-concept."

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The Psychosocial Worlds of the Adolescent: Public and Private, by Vivian Center Seltzer. New York, John Wiley & Sons, 1989, 278 pp., \$39.95.

In a world where young adolescent girls can still be sold into slavery or be sexually abused and where millions of children and adolescents are starved by hunger or dislocated by war, it is not surprising that international leaders have gathered for a world summit on children. Not only is this the decade for the child and adolescent, but it is also an opportunity to learn more about that transitional period between childhood and adulthood known for its impetuosity and passion. One such lantern for academic or clinically oriented readers into the arcane world of adolescence and its peer-to-peers interface is Vivian Center Seltzer's *The Psychosocial Worlds of the Adolescent*.

Dr. Seltzer, an associate professor of human development and behavior at the University of Pennsylvania, succinctly states that her book is "about the manner in which adolescents view and use their greater social world, the primary position and developmental value of the peer in it, their reciprocal psychosocial interactions, and how they operate for and against one another in accomplishing the psychosocial task of achievement of identity." To this end Professor Seltzer puts together a six-part text that explores the many dimensions in which adolescents affect each other's psychosocial growth. From their imperative to be together to the dynamic of the

"adolescent dialectic," she dissects the emotional pulling from both childhood and young adulthood.

After a brief historical overview recapitulating the major ideas surrounding the adolescent period and setting the tone for subsequent chapters, Dr. Seltzer, in part two, offers "an alternative orientation" to interpreting adolescent behavior called "dynamic functional interaction." Issues of conformity, friendships, social preference, etc., underscore the key dynamic of the adolescent period and a major component of dynamic functional interaction. This dynamic, also named the "comparative act," is ever-vigilant; it begins the process of establishing the self or the identity. Every feature, from one's skin turgor to the number of facial comedones, from one's sports skill to one's ability to dance, is frenetically compared with those of other peers. Comparison leads to the integration and refinement of self-elements and ultimately to identity crystallization. Consequently, adolescents must have access to peers—"being with one another, looking, listening, and . . . comparing." The multiple complements of age mates, which not only form interdigitating and divergent groups but also allow for the "comparative act," become the "peer arena."

Parts three, four, and five, approximately two-thirds of the text, provide the empirical basis and findings based on nine psychosociometric instruments collectively called the Peer Progression Battery. This battery samples adolescent public and private socialization preferences and practices. The results of this battery support the dynamic functional interaction notion of the "peer arena" and suggest some intervention strategies for adolescents whose progression in growth is not smooth.

The final part of the book highlights some of the practical applications of the preceding chapters' empirical findings and theories. Specifically addressed are suggestions for "parenting, education and counseling, and healing." All interventions emphasize the importance of the "peer arena" and the "comparative act."

In summary, *Psychosocial Worlds of the Adolescent* is a well-written and well-researched tome dealing with a predominately middle-class, white U.S. adolescent population. Although oversubscribing to the Jesuit notion that repetition is the mother of learning, especially regarding the thesis that the "central developmental figure" of adolescence is the peer, the text effectively uses the pedagogic tools of summaries at the beginning of the sections, an introduction and an end note, a list of references, and both an author and a subject index. Nevertheless, if you are not interested in either research methodology or psychosociometric instrumentation, you will find this work both verbose and repetitive; the new ideas are useful and heuristic, but they could easily be condensed into a thoughtful essay.

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ALZHEIMER'S DISEASE AND DISORDERS OF MEMORY

Familial Alzheimer's Disease: Molecular Genetics and Clinical Perspectives, edited by Gary D. Miner, Ralph W. Richter, John P. Blass, Jimmie L. Valentine, and Linda A. Winters-Miner. New York, Marcel Dekker, 1989, 408 pp., \$125.00.

There is no doubt that Alzheimer's disease is an inherited behavioral disorder, but both clinicians and researchers face an array of unanswered questions concerning the genetic basis

of this dementia syndrome. What is the pattern of inheritance for Alzheimer's disease? What is the *mechanism* of the inheritance? Is it polygenic? How should we understand sporadic cases, familial cases, and variable onset ages? *Familial Alzheimer's Disease* aims to provide selected reviews of current research into such questions regarding the genetics of Alzheimer's disease.

This edited volume has emerged from an almost 20-year effort by the Familial Alzheimer's Disease Research Foundation in Tulsa, Oklahoma, to provide support for families at risk for Alzheimer's disease. Four of the five editors are based in Tulsa, and all are involved with Alzheimer's disease, either clinically or in research. Other contributors to the book, however, have been solicited widely from national and international research centers.

Section one of the book reviews clinical evidence suggestive of a genetic basis for Alzheimer's disease. Such issues as neuropsychological patterns in familial versus nonfamilial Alzheimer's disease as well as epidemiologic and twin studies are reviewed. Section two takes on the daunting task of providing an overview of current molecular genetic research in Alzheimer's disease. Issues of research methods are reviewed in some detail. I found the chapter by Dr. St. George-Hyslop et al. concerning genetic linkage studies and amyloid precursor genes on chromosome 21 to be especially helpful as an overview. In the third section, potential lines of research development in Alzheimer's disease are reviewed. Neuropsychological issues are revisited in a chapter prepared by the editors. The theoretical basis for possible palliative therapies using peptide replacement or trophic factors is reviewed by Drs. Giacobini and Becker from Southern Illinois School of Medicine. The usefulness of new cerebral imaging modalities in diagnosis is considered in another chapter, and peptides, calcium metabolism, and neuroimmunological issues are considered in others. A brief fourth section of the book considers more global research and legal matters.

The book is attractive and modest in size. The price is high. Research in Alzheimer's disease currently spans a broad frontier, and only a sample can be included in such a work. The volume would be of greatest interest to clinical or basic investigators who have special interests in the genetics of Alzheimer's disease. Clinicians dedicated to dementia programs might also wish to buy the book as a background or reference instrument.

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Alzheimer's Disease: Treatment and Long-Term Management, edited by Jeffrey L. Cummings and Bruce L. Miller. New York, Marcel Dekker, 1990, 380 pp., \$125.00.

Approximately two million Americans suffer from Alzheimer's disease, a tragic, unrelenting dementing illness that culminates in death. At a time when the field of geriatrics is exploding with new insights, this text organizes and evaluates the treatment and management of Alzheimer's disease. It does so primarily through the presentation and scrutiny of current clinical research data.

There are 25 separately authored chapters, with topics ranging from basic neurochemical theory and research to clinical psychopharmacology, behavioral management, and national policy issues. Many of the chapters presume the reader has a good understanding of neurophysiology and psychopharmacology. The chapters are grouped into five sec-

tions, each prefaced by a concise introduction by the editors. The first section, Introduction, has one chapter, "Clinical Diagnosis of Alzheimer's Disease," authored by Dr. Cummings. This is an excellent review that emphasizes the use of specific clinical features as well as exclusionary criteria when making the diagnosis of Alzheimer's disease.

The second section, Disease-Specific Therapies, explores pharmacological treatments of Alzheimer's disease. These treatments have their basis in postulated and observed neurophysiological abnormalities seen in the disease. Acetylcholine replacement and augmentation, ergoloid mesylate treatment, and other pharmacological interventions are critically reviewed. The data presented indicate that no agent has been shown conclusively to modify the course of Alzheimer's disease, so perhaps Evaluation of Disease-Specific Therapies would have been a more appropriate title for this section.

The third section, Treatment of Behavioral Symptoms, is an informative review of the medications often used to treat such common manifestations of Alzheimer's disease as agitation, combativeness, and suspiciousness. The use of neuroleptics, α -blockers, antidepressants, and other agents is critically evaluated. This section should help the physician working with demented patients to make informed decisions regarding psychopharmacological interventions.

Long-Term Care, the fourth section, is a collection of chapters focusing on a variety of issues, including wandering, incontinence, and medical complications of dementia. Behavioral as well as pharmacological treatments are explored. Psychosocial measures to aid the families of Alzheimer's victims are discussed because family members, not long-term care facilities, provide the bulk of primary caretaking to demented individuals.

The final section, Future Treatment Directions, speaks to potential new treatments such as cholinergic enhancement, neuropeptide manipulation, genetic engineering, and tissue grafting. Overall, I found this section to be the weakest of the five. There is a considerable amount of overlap with material presented in the second section as well as a distinct departure from the clinical arena to more basic neurochemical and neuroanatomical principles. The final chapter touches on the massive financial burden of long-term care for those suffering from Alzheimer's disease and the need for comprehensive measures to cope with this national crisis.

In summary, this text is a thorough, up-to-date, scientifically minded, medically oriented, and clinically useful review of Alzheimer's disease. It successfully organizes and integrates material in a wide and rapidly expanding field. The editors intend this book to serve as a practical manual for the treatment of dementia, and it surely meets that goal; however, some readers may find the time spent on basic research issues excessive.

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Human Organic Memory Disorders, by Andrew R. Mayes. New York, Cambridge University Press, 1988, 300 pp., \$52.50; \$18.95 (paper).

Delirium: Acute Confusional States, by Zbigniew J. Lipowski, M.D., F.R.C.P. (C). New York, Oxford University Press, 1990, 478 pp., \$69.50.

These two books discuss, in a most comprehensive fashion, two of the most common and major problems confronting general hospital psychiatrists—delirium and memory dys-

function. Both are excellent books. They make one wish that senior behavioral scientists would summarize their major interests in monograph form so that we could have a comprehensive library of psychopathological syndromes and phenomena.

Human Organic Memory Disorders is a clear and comprehensive book on a most difficult subject. The difficulty of the subject is attested to by the fact that it is necessary to include a glossary of the highly technical and somewhat idiosyncratic terms used in the study of memory. The book is divided into nine chapters: 1) "Healthy and Pathologic Memory," which also includes a nice review of the neuroanatomy of areas associated with memory function, 2) "The Assessment of Memory Disorders," 3) "Disorders of Short Term Memory," 4) "Disorders of Previously Well Established Memory" (long-term memory), 5) "The Memory Problems Caused by Frontal Lobe Lesions," 6) "Organic Amnesia," 7) "Animal and Biochemical Models of Amnesia," 8) "Less Well-Characterized Memory Disorders," which covers most of the neurological and psychiatric syndromes that have had reported memory impairments such as schizophrenia, depression, Huntington's disease, and multiple sclerosis, and 9) "Overview."

The book presents very current research on memory functions and is quite refreshing and candid in presenting most of the data as supporting hypotheses that have yet to be proven. The author covers not only semantic memories but also memory related to motor function and presents an interesting hypothesis about dyspraxias, aphasias, and agnosias as defects in memory function. These motor aspects of memory are seldom considered, but there certainly are motor and sensory memories that are stored in the brain as well as perceptual experiences. For instance, having once learned to ride a bicycle, we seem always able to do it.

It is still unclear whether the many types of memory defects listed in each of the separate chapters are defects in registration, storage, or retrieval of information. Many of the memory dysfunctions are discussed in terms of single case studies, which always leaves one wondering about the generalizability of the findings. However, the book is an excellent review of the current state of memory research and, although difficult, would be worthwhile for every psychiatrist interested in this area, as well as most trainees, to read. The only criticism that can be made of this excellent monograph, which is balanced and circumspect, is that it is based too much on the historical organization of the brain (e.g., frontal lobe, parietal lobe, temporal lobe, etc.) and not at all in keeping with current concepts of neurophysiology related to parallel processing and functional loops rather than attempts to localize memory disturbances based on these historical anatomical distinctions.

In 1967, Dr. Lipowski (1) published one of the best single papers in descriptive psychiatry on delirium. In 1980 he published a definitive monograph that was a massive expansion of this paper (2). Fortunately for us, in 1990 he updated this comprehensive monograph, which is basically the same book now entitled *Delirium: Acute Confusional States*. To give the scope of this book, it is best to quote Dr. Lipowski, who notes in the chapter on the history of delirium,

This historical account covers 2,500 years. It documents an unbroken continuity of the clinical descriptive concept of delirium over the centuries despite the confusing vagaries of relevant terminology. The history of this concept underscores the value of clinical observation as the empirical cornerstone of progress in both medicine and psychiatry. Moreover, it constitutes an important chapter not only in the history of those two

fields, but also in the development of ideas about the nature of humanity, of mind, and of the mind-body relationship. (p. 34)

In truth, Dr. Lipowski's excellent monograph lives up to this summary.

Part one is entitled *Delirium: An Organic Mental Syndrome* and includes chapters on the history of delirium; definition of terms; incidence and prevalence; clinical features, course, and outcome; psychopathology; etiology; pathogenesis and pathophysiology; diagnosis; differential diagnosis; and treatment. Part two contains chapters that cover organic causes of delirium such as intoxication, poisons, alcohol and drug withdrawal, metabolic disorders (encephalopathies), infections, vascular diseases, head injury, epilepsy, and brain tumor. Part three covers delirium in special patient populations such as geriatric, postsurgical, burn, and childbirth patients.

Not only are the references completely up-to-date, but the author covers a good deal of the recent data from the use of modern imaging techniques to elucidate the etiology of delirium. The book is highly readable and extremely useful, more perhaps as a reference than as something one would read straight through, but it should be on the shelf of every general hospital psychiatrist. If any criticism could be made of this book, it is that, as with any extensive literature review, there is often an uncritical presentation of the comprehensive material included, thus leaving one with the feeling that everything is important. However, this is a minor criticism of a fine book.

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SLEEP AND ALERTNESS

Sleep and Alertness: Chronobiological, Behavioural, and Medical Aspects of Napping, edited by David F. Dinges and Roger J. Broughton. New York, Raven Press, 1989, 346 pp., \$116.50.

In *The Posthumous Papers of the Pickwick Club* (1837), Charles Dickens elegantly described the sleep episodes of the fat boy Joe, who showed all of the features of what came to be called the Pickwickian syndrome. Some of its symptoms, like daytime sleepiness and napping, were not shown to be related to obstructive sleep apnea until more than a century later.

This highly informative volume reviews what is known about the significance and utility of napping. The editors regard sleep as a central mystery of evolution as well as one of the most pervasive behavioral controls in nature. Sleep can dramatically affect the quality of being awake. In the research on the sleep/wake cycle, napping has been "sleep's orphan" in that it has received little coherent or integrated analysis since the beginning of modern sleep research by Kleitman and co-workers some 30 years ago. It has often been considered a deviant and unwanted form of sleep, indicative of laziness, irresponsibility, immaturity, or senility. Napping can also be

considered healthy and appropriate, however. The universal presence of napping across species and ages indicates its biological importance.

This book provides data concerning napping from many perspectives. The study of the development of human napping is most important for clinicians and scientists trying to unravel the nature of sleep, sleep disorders, and chronobiology. Research on napping in time-free environments indicates its endogenous character. The timing of naps appears to be tied to the circadian rhythm governing the subject's core temperature. The chapter on daytime napping in cultures that incorporate the siesta would have been more fascinating had it been more up-to-date.

The chapter entitled "Sleep Attacks, Naps, and Sleepiness in Medical Sleep Disorders" is most interesting. Broughton has done extensive studies of the *maladie de Gélinau*, commonly known as narcolepsy. Both sleep attacks and naps are refreshing and followed by greater alertness. None of the classical hypersomnias has been found to be attributable to a primary disturbance of sleep/wake biorhythms. They all show relative preservation of the main circadian, circasemidian, and ultradian sleep/wake features characterizing normal sleep. In narcolepsy, the REM-based symptoms of cataplexy, sleep paralysis, hypnagogic hallucinations, and nightmares normally respond well to tricyclic medication such as imipramine, clomipramine, and monoamine oxidase inhibitors. Nocturnal γ -hydroxybutyrate is also effective in ameliorating the fragmented REM sleep of narcolepsy.

If napping is a fundamental human behavior, it is not certain how and why it came to be so. The bulk of data obtained from a variety of approaches, such as nap patterns at different ages, ultradian sleep ability, napping during temporal isolation, and napping among shift workers, all strongly support the existence of a biphasic sleep pattern.

Social forces in modern societies suppress napping. A critical function of napping in such societies could be to reduce daytime sleepiness and enhance alertness. Whether maintaining a biphasic sleep/wake cycle is really important for health and functioning remains uncertain, however. The editors seem to long for a revival of napping.

This well-referenced book will be stimulating to anyone who is interested in research on sleep and alertness, although the price could be a problem. It deserves a place in the library of all psychiatric institutions.

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BEHAVIORAL MEDICINE

The Practice of Behavioural Medicine, edited by Shirley Pearce and Jane Wardle. New York, Oxford University Press, 1989, 307 pp., \$75.00.

This edited volume attempts to put in context the concepts and approaches of behavioral medicine in health and illness. In the introduction, the editors state many of the premises of behavioral medicine and the conceptual basis on which the field approaches the interface between psychological issues and medical disorders. For example, behavioral treatments and techniques, such as relaxation, biofeedback, stress management, and life style changes, may be useful for a wide range of clinical problems and disorders and are not necessarily disorder specific. The authors exert more effort on the examina-

tion of etiology (mechanism) than application and focus on the concept that the medical model is insufficient to fully explain or to manage medical disorders. In addition, they identify the following recurrent themes in the book: techniques of improved behavioral assessment (more effective instruments), liaison with other health care providers to convince them of the merits of their approaches, adherence and compliance with prescribed medical protocols, the impact of psychosocial issues on the occurrence and treatment of medical illness, and the investigation and application of techniques to influence life style changes in the service of disease prevention and disease treatment.

From the editors' point of view, the concept of the medical model has limited the evidence for etiology (mechanism) and treatment for many maladies. An expanded conceptual framework is therefore mandatory: a psychosocial model applied on top of the core biology. The editors indicate that this integrated model began with two important events: 1) the first Behavioral Medicine Conference at Yale in 1977, which many view as an important historical watershed because a journal, a society, and federal funding followed, and 2) the establishment of the Health Psychology 38 Division within the American Psychological Association by Matarazzo and others.

The editors selected pragmatic issues to serve as illustrations of the application of behavioral medicine. Some of the chapter authors were asked to present what is known about the behavioral management of discrete medical disabilities such as hypertension, diabetes, and obesity and to describe specific approaches to these disabilities. Others were selected because they offered specific management strategies for cardiac rehabilitation, chronic pain, HIV infection, or smoking cessation. This range of medical disorders and their approaches by practitioners of behavioral medicine shows other mental health workers how behavioral medicine is applied. The book was not designed to be an encyclopedia of the field. Rather, it is a handbook and "how-to" volume for those wanting to know about the discipline. It is an important work for psychiatrists who may not be sufficiently familiar with the techniques and strategies described, although they may have some feeling about the patients being referred to as "clients."

Each chapter is organized so that background data on the subject in question, including epidemiology and morbidity, are given first, followed by the goals of rehabilitation, behavioral interventions for the disability, case histories with intervention strategies, and, in certain instances, examples of the application of behavioral techniques from a particular center. It may be that this design is too ambitious in that the scientific database for the disorder is by necessity presented in too limited a fashion for a practitioner in that medical domain.

In the chapter on hypertension, the authors underscore the need for accurate biological assessment and offer guidelines for how, when, and by whom blood pressure should be measured. This emphasis on careful biological measurement is essential. Then they move to who should be treated with behavioral modalities and when. One might disagree with the suggestion that "if it [blood pressure] regularly reaches a level beyond the 'mildly hypertensive' range (above 170/105 mm Hg), the referring physician should be informed, and the possibility of pharmacological treatment considered." Some might incorporate pharmacological treatment even in this more mild form of hypertension and not wait for it to reach the 105 cutoff level.

Although the authors provide a "how to" for the behavioral treatment of obesity, salt and alcohol intake, and lack of ex-

ercise, they do not describe adequately controlled studies of interventions using random samples and followed over prolonged periods of time. In fact, one would question the authors' statements that a 4.4-lb weight loss in 4 years is substantial and that alcohol consumption equal to 2 quarts of beer a day does not need modification and their almost elective use of Alcoholics Anonymous for problem drinkers. The behavioral modification to enhance exercise seems quite pedestrian. The second major strategy to reduce stress is described in a very elementary way.

In the chapter on cardiac rehabilitation, the physiological and pathological background is at a very basic level for physicians and appears to be designed for nonmedical health care workers. Another concern is that there is minimal critique of the data presented as background. Is the depression noted by these sources a mood disturbance or a major affective disorder, and did these studies have random controlled designs? Many of the references cited are not current. Langosch recommends that the psychologist adopt a liaison posture with regard to the cardiac team and describes the approach of his cardiac rehabilitation center. "It is also essential that psychologists working in this area have a firm knowledge of basic cardiologic terms and mechanisms," he says (p. 30). He offers no place for the psychiatrist on the cardiac consultation-liaison team. The validity of the multiple assessment measures suggested is not questioned in the medically ill cardiac patient, nor is the need to modify the instruments measuring disturbances of mood in the medically ill. In addition, there is no mention of the prescription of psychotropic medications during acute and follow-up coronary care, although the author takes great pain to describe cognitive-behavioral interventions for patients who are to receive cardiac catheterization. A carefully documented approach to reeducate and modify high-risk behavior and attitudes addresses smoking, nutrition, exercise, relaxation, and stress coping strategies. However, there is no mention of evaluation for the organic mental disorders that can accompany medical disorders (axis III disorders), the drugs prescribed to treat them, or any role for a psychiatrist in assessment or intervention.

In the chapter on injury to the CNS, Wilson underscores the importance of assessment, discusses the different behavioral paradigms to be used, and gives case illustrations of these behavioral approaches in great detail.

Pearce and Erskine offer a comprehensive review of pain theories, assessment measures, and psychological interventions for chronic pain, such as contingency management operant methods, cognitive methods, relaxation, and biofeedback. However, long-term outcomes are poorly described, including the model presented in detail.

The chapter on counseling in HIV infection and AIDS does not take up the issue of suicide, nor does it describe many of

the findings in the United States with regard to the changes in behavior after counseling. The refractoriness to behavioral change in the intravenous drug abuser versus the gay patient with HIV positive results is not explored.

In her chapter on the management of obesity, Wardle presents many concepts regarding weight regulation that are challenged by current data. For example, she states that individuals have a fixed weight (setpoint theory), that intermittent dieting may have a lasting effect on decreasing basal metabolic rate, and that obese persons do not overeat. This may have influenced the deemphasis on alterations of the diet that are viewed as "restrictive," although the behavioral elements of the treatment strategy presented are based on current knowledge.

Thornton offers a thoughtful review of research pursuits in the irritable bowel syndrome. The chapter on respiratory disorders emphasizes the role of the patient as an active partner in the treatment of such afflictions through the performance of self-management skills and serves as a paradigm for patient participation, which is clearly an issue in need of development.

Finally, Jarvis' review of smoking cessation programs emphasizes the role of nicotine dependence, the need to overcome recidivism, and the use of time-limited interventions. The recurrent approach to the smoker, with full awareness that most will require several attempts to stop, and the adjunctive assistance of nicotine replacement (in the form of gum) may have the greatest potential for success.

We are indebted to the editors and authors of this book for bringing the practice of behavioral medicine succinctly into focus in one volume. They have highlighted their approach for specific maladies in a pragmatic fashion and offered a "window" on the operations of the psychologist in this important arena. Unfortunately, insufficient data documenting long-term gain from the efforts extended for both the patient and the health care team are presented for the majority of the interventions. Behavioral medicine offers many promising approaches to the treatment of medical illness, but the next wave of effort in behavioral medicine might focus on outcome studies, not only of the long-term effectiveness of the intervention but of expenditures of time and costs as well. Once such data are available from controlled studies with rigorous methodological designs (including reliable and valid instruments for measuring mental disorders), it should be possible to secure increased funding from third-party payers for the interventions the authors so carefully describe. Another generation of studies also needs to be undertaken to discern in which setting and by whom such interventions can be provided with the maximum cost savings.

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Reprints of Book Forum reviews are not available.

Safety of Short-Acting Benzodiazepine Hypnotics in Patients With Impaired Respiration

SIR: Although in recent years there has been increasing attention to various aspects of the widespread use of benzodiazepine sedative/hypnotics, there has been relatively little written about the possibility that they may depress respiration during sleep. This is of particular concern with long-acting benzodiazepines, which may decrease respiratory drive and increase P_{CO_2} in patients with chronic obstructive pulmonary disease (1) and enhance apneas in patients with even very mild sleep apnea (2) and in elderly normal subjects (3). Such patients may become more sleepy, irritable, or forgetful in the daytime; it is possible to misconstrue these symptoms of sleep apnea as part of a patient's pathology or as a drug's residual sedative effect. It is not clear whether respiratory depression occurs with short-acting benzodiazepines. We have recently had an opportunity to assess the effects of these agents on insomniac patients who suffer from both nocturnal myoclonus and mild sleep apnea.

These eight male, middle-aged patients presented with complaints of chronic insomnia and were found to have a mean \pm SD of 165.7 \pm 91.9 periodic leg movements that disrupted their sleep. In uncomplicated cases, the typical treatment would include administration of a benzodiazepine such as clonazepam. In addition, however, these individuals had mild sleep apnea, with a mean \pm SD of 35.5 \pm 41.2 disordered breathing events (apneas plus hypopneas) in non-REM sleep and 9.2 \pm 9.5 in REM sleep. These events were of mixed type (64% obstructive), with mean durations of 22–27 seconds.

Because of the degree of distress experienced by these patients, we agreed to treat the myoclonus with short-acting benzodiazepines, using a laboratory setting to observe possible effects on respiration. Seven patients received triazolam, 0.25 mg, and one received lorazepam, 4 mg.

As has been reported by others, there was some disparity between objective and subjective reports of benefits of the benzodiazepines for these patients. Although the number of periodic leg movements decreased only slightly to 144.0 \pm 106.4, the patients described benefits of the drugs. We found no evidence to suggest that drug treatment altered sleep-related respiration. The number of disordered breathing events during the drug condition was 43.5 \pm 49.6 in non-REM sleep and 4.9 \pm 6.9 during REM sleep. The mean minimum arterial oxygen saturation, which ranged from 88% to 91% in the baseline condition, was 86%–90% after patients received the hypnotics. The mean duration of disordered breathing events, which ranged from 22 to 27 seconds in non-REM and REM sleep, respectively, at baseline, was 15 and 21 seconds after they received the drugs. Paired *t* tests revealed no statistically significant drug effects on any of the measures of respiration.

To assess whether degree of severity affected drug response, the patients were divided into the four with the highest and the four with the lowest numbers of disordered breathing events in non-REM and REM sleep. There was no trend or significant difference between the two groups in the frequency of a decrease in these events.

These data indicate that short-acting benzodiazepines do not acutely alter sleep-related respiration in patients with mild mixed apneas. A recent report suggested that triazolam may actually improve respiration in patients with mild central apnea (4), possibly by reducing brief transitions to wakefulness that may be associated with changes in respiratory control. A previous report by Guilleminault et al. (5) also indicated that clonazepam reduced apneas in patients with nocturnal myoclonus and central sleep apnea. At this point, clear clinical guidelines await further study of dose responsiveness and effects of chronic administration. These studies suggest, however, that the clinician may base the decision to prescribe these agents on their relative indications and contraindications, with less concern that sleep-related respiration will be compromised.

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Intravenous Dexamethasone for Symptoms of Major Depressive Disorder

SIR: Although much has been written regarding the hypothalamic-pituitary-adrenal (HPA) axis and its dysregulation during depression (1, 2), there are, to date, no clinical studies of the use of glucocorticoids in major depressive disorders (3). We have given patients with DSM-III-R major depression 4 mg i.v. of dexamethasone in an uncontrolled, nonblind design and assessed their symptoms before injection and 7 days following injection.

The five patients we selected were men between the ages of 25 and 65 years (mean \pm SD=50 \pm 10 years) recruited from an outpatient psychiatry clinic. They met the criteria for the diagnosis of major depression, as determined with the Structured Clinical Interview for DSM-III-R (SCID). They had no active medical illness or other concomitant psychiatric illness or substance abuse and were medication free. The criterion

for entry into the study was a score greater than 20 on the Hamilton Rating Scale for Depression. Following psychiatric evaluation, the patients received 4 mg i.v. of dexamethasone over a 10-minute period in 10 cc of normal saline administered through a mechanized pump (Harvard pump). The Hamilton depression scale was given on the morning before injection and 7 days later at the same time of day. Seven normal male comparison subjects with no psychiatric diagnosis were also evaluated after they received 4 mg of dexamethasone intravenously.

None of the depressed patients reported mood alteration or euphoria in the several hours following the injection or in the 24 hours following the infusion. The patients had a mean \pm SD Hamilton depression score of 29.4 \pm 4.5 on day 1 prior to the infusion, and on day 7 after the infusion the mean score was 13.6 \pm 4.6 ($t=4.87$, $df=4$, $p<0.008$, two-tailed test). Four of the five patients showed more than a 50% reduction in Hamilton depression score (mean=65%), and one patient demonstrated only a 20% reduction. Six of the normal comparison subjects reported no elevated mood, and one reported a transient "good feeling" for an hour following the injection. None of the comparison subjects had euphoric mood or elevated mood in the week following the injection.

The depressed patients showed clear improvement after receiving the infusion of dexamethasone. As with any report of five patients responding to a novel treatment, controlled clinical trials are imperative for validation of the effect. We did not have any data on these individuals regarding HPA status (urinary free cortisol, results of dexamethasone suppression tests, etc.). A recent report (4) presented data on normal volunteers who received prednisone for 5 days and demonstrated clear effects on HPA axis parameters as well as alterations in mood and behavior. Although the mood-elevating effects of glucocorticoids can be suspected in this finding, the fact that in our study, six normal comparison subjects felt no euphoric effects and none of the patients reported feelings of euphoria or a "high," makes this unlikely as the reason for the clear improvement in depressive symptoms.

In summary, four of five depressed men showed marked improvement in depressive symptoms after receiving intravenous dexamethasone. These patients were taking no concomitant medications and had been depressed for at least 2 weeks before the dexamethasone infusion. More studies need to be undertaken in which this strategy is pursued in nonpsychiatric and psychiatric comparison subjects and patients are given intravenous dexamethasone in a placebo-controlled, double-blind design, with measurements of cortisol and dexamethasone before and after treatment.

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Acute Exacerbation of Chronic Schizophrenia in a Patient Treated With Antituberculosis Drugs

SIR: Isoniazid is an antituberculosis agent able to produce a broad variety of side effects, including hepatitis and neurological toxicity (1). Among the neurological side effects are peripheral neuritis, seizures, optic neuropathy, memory dysfunctions, and toxic psychosis (2, 3). We describe a patient who suffered an acute relapse into chronic schizophrenia, residual type, according to the *DSM-III-R* criteria, soon after starting isoniazid and other antituberculosis drugs.

Ms. A was a 30-year-old unemployed woman with an irrelevant past medical history, a schizoid premorbid personality, and a large family history of psychosis. She had been admitted to a hospital for the first time at the age of 22 because of an episode of hallucinations and delusions. A diagnosis of schizophrenic psychosis, paranoid type, was made according to the *DSM-III-R* criteria. She was treated with trifluoperazine, 5 mg/day, during the next 7 years. Apart from some negative symptoms such as social isolation and inappropriate affect, she remained asymptomatic.

At the age of 29, Ms. A was diagnosed as having cervical lymph node tuberculosis (*Mycobacterium tuberculosis* was grown in prurient material spontaneously draining from the lymph node). She weighed 45 kg. The involved lymph nodes and the underlying sinus tracts were excised, and isoniazid, 225 mg/day; rifampin, 450 mg/day; and pyrazinamide, 1200 mg/day, were started. The HIV serology was negative.

Five days later Ms. A had to be admitted to the hospital because of progressive psychomotor agitation, unusual and bizarre behavior, auditory hallucinations, and delusions of control and of being possessed. There was no clouding of consciousness, and she was cognitively intact. Ethambutol was substituted for isoniazid, and trifluoperazine was started, with increasing doses until the dose reached 25 mg/day. The delusions and auditory hallucinations disappeared progressively.

To our knowledge, pyrazinamide and rifampin have not been associated with psychotic side effects, whereas isoniazid has been identified as a triggering factor for the onset and relapse of schizophrenia, probably due to its activity as a monoamine oxidase inhibitor (4). The onset of a psychosis in a healthy individual treated with isoniazid is very infrequent unless doses as high as 15 mg/kg per day are used. It is possible, however, that the usual dose of 5 mg/kg per day could be enough to trigger a relapse in patients with psychosis. We conclude that isoniazid should be used with caution in patients with histories of psychotic disorders.

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Persistent Dyskinesia in a Patient Receiving Fluoxetine

SIR: Recently, there have been several reports of extrapyramidal symptoms resulting from fluoxetine (1-3). In most cases, however, neuroleptics had been either administered concurrently or only recently discontinued. We report the case of a woman with schizoaffective disorder, with remote exposure to neuroleptics and no previous history of movement disorder, who developed buccal-lingual dyskinesia after an 8-day course of fluoxetine alone.

Ms. A was a 43-year-old woman who had first been hospitalized at age 23 for depression and psychosis. She received several neuroleptics as well as amitriptyline and ECT. After several months she discontinued medication, and she remained in stable condition for 7 years. She then experienced recurrent symptoms, which were treated with combined low-dose neuroleptic and amitriptyline. She remained stable without taking medication for a year, until she was treated briefly with low-dose neuroleptic alone for psychosis.

Ms. A remained asymptomatic without taking any medication for the next 7 years until psychotic symptoms recurred and were treated with trifluoperazine, 4 mg/day, for 2 weeks. This was her last exposure to neuroleptic medication. She remained stable without any medication for another 4 years.

At age 43 Ms. A received lithium, 1200 mg/day, for 6 weeks for hypomania. She was next seen 3 months later, when she was treated for depression with fluoxetine, 10 mg/day for 5 days, followed by 20 mg/day for 3 days. She then developed abnormal, involuntary choreiform movements involving the tongue, jaw, and mouth. Her tongue was observed to dart back and forth across her teeth, and it also rolled and curled laterally. There were sucking and blowing movements of her cheeks and intermittent clenching of her teeth. These movements kept her awake at night. Fluoxetine was discontinued, and within 10 days the movements began to subside, although 8 weeks later the movements were still apparent. At 12 weeks the movements were minimal and involved only her tongue. They were elicited primarily with activity, and the patient complained that they worsened during times of stress or anxiety.

It should be noted that this patient had no previous history of abnormal movements, cardiovascular or cerebral disease, or dental problems and demonstrated no other abnormalities upon neurological examination. After fluoxetine was stopped, she refused further treatment except for vitamin E, 400 IU/day. Her depressive symptoms resolved spontaneously within the following 2 weeks, but her abnormal involuntary movements persisted, although with progressively less severity than at initial presentation.

Neuroleptics and lithium have been associated with various dyskinesias, including tardive dyskinesia. Patients exposed intermittently to neuroleptics and patients with affective illnesses seem more vulnerable to this complication of treatment (4, 5). For this patient, treatment with neuroleptics was sporadic, brief in duration, and at low doses. She had not received any neuroleptic for 4 years prior to developing abnormal involuntary movements after taking fluoxetine.

Prior exposure to neuroleptics and/or lithium may sensitize nigrostriatal dopaminergic responses to increased serotonergic input from the raphe nuclei. Alternatively, abnormal involuntary movements may result from direct modulation of serotonergic input at the level of the subthalamic nucleus.

However, the noteworthy feature in this case is the first onset of tardive dyskinesia-like movements only after exposure to fluoxetine alone.

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Fluoxetine-Induced Mania in a Patient With Obsessive-Compulsive Disorder

SIR: It has recently become clear that like other antidepressants, fluoxetine has the potential to induce mania or hypomania in depressed patients. Eight cases of fluoxetine-induced mania have been reported in patients with unipolar depression (1-3) and one case in a patient with panic disorder (4). To our knowledge, fluoxetine-induced mania in patients with other forms of psychiatric illness has not been reported. We describe the development of hypomania in a patient with obsessive-compulsive disorder following the use of fluoxetine.

Ms. A, a 42-year-old woman, had a 5-year history of moderate obsessions and compulsive rituals. Initially, she had been unsuccessfully treated with a low dose of clomipramine. At home her cleaning rituals took 3-4 hours a day, and at work she spent 3-6 hours a day cleaning bathroom stalls, ruminating about dirt on the bathroom walls and in her apartment back home. The symptoms were ego-dystonic and disturbing to the patient. She had no delusions or hallucinations. Her mild dysphoria seemed to be associated with her obsessive-compulsive disorder. She had no vegetative symptoms of depression and did not fulfill *DSM-III-R* criteria for affective illness. There was no personal or family history of bipolar disorder or mania.

Ms. A was started on a regimen of fluoxetine, 20 mg p.o. each morning, and within 4 weeks devoted only 20 minutes a day to cleaning rituals and obsessive ruminations. Six weeks after starting fluoxetine, she presented to the clinic with pressure of speech and logorrhea. She was disheveled, was dressed in uncharacteristically bright colors, and wore excessive makeup. She complained of racing thoughts and difficulty in "slowing down" and said that she felt better than she had in years and had decided to borrow a large amount of money. Her sleep was normal. Because of her hypomanic behavior, her dose of fluoxetine was lowered to 20 mg every second day. After 2 weeks, Ms. A had become euthymic and her obsessive-compulsive symptoms were under control.

After 4 weeks of the decreased dose, the obsessions and

ritual behavior recurred. Fluoxetine was again increased to 20 mg/day, and clonazepam, 0.5 mg p.o. at bedtime, was added to prevent the recurrence of hypomania. Two weeks later Ms. A had no rituals or obsessive thoughts and was euthymic. After 2 months, the dose of clonazepam was lowered to 0.25 mg p.o. at bedtime, and the patient has continued to take this dose in combination with fluoxetine, 20 mg/day, for the past year with no recurrence of obsessive-compulsive or hypomanic symptoms.

In the initial case reports of fluoxetine-induced mania, all of the patients suffered from a primary affective illness, making it impossible to determine whether fluoxetine had uncovered a latent bipolar illness or was by itself capable of inducing mania. The recent report of mania in a patient with panic disorder suggests that fluoxetine is capable of inducing mania in patients with no preexisting mood disorder. Our case further supports this hypothesis. As the use of fluoxetine becomes more widespread, all patients, regardless of primary psychiatric diagnosis, should be monitored for the development of mania. To prevent this switch in patients with obsessive-compulsive disorder, one should consider initially using the low doses that were effective in this case rather than the higher doses reported elsewhere (5).

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Mania Induced by Fluoxetine in an Adolescent Patient

SIR: Several cases of mania precipitated by fluoxetine have been reported in adult patients. These patients were either known to have bipolar disorder (1, 2) or thought to have unipolar depression (1-3). The experience with fluoxetine in children and adolescents remains limited. We report case of mania induced by fluoxetine in a male adolescent patient. To our knowledge, this has not been reported before.

Andrew, a 15-year-old boy with no past psychiatric history, had been depressed for several months, becoming withdrawn at school and at home. He complained of low energy and entertained thoughts about death. Other symptoms included decreased concentration and school performance, difficulty falling asleep, and early morning awakening. His appetite remained unchanged. His grandfather had had a diagnosis of schizophrenia and had committed suicide.

On examination, Andrew had poor eye contact and appeared confused at times. His affect was depressed and his speech was minimal and latent. He denied being suicidal. Further observation revealed some loosening of association

and delusions. He was admitted to the hospital with a provisional diagnosis of major depression.

The results of psychological tests, including the Draw-a-Person, Rorschach, Thematic Apperception Test, and Milon Adolescent Personality Inventory, demonstrated significant depression, schizoid traits, and personalized thinking that approached a psychotic level.

Desipramine was started and increased to 150 mg h.s. Thioridazine was also started and increased to 150 mg, but it was stopped 3 weeks later because of side effects. Thiothixene was used instead, and the dose was gradually increased to 20 mg b.i.d. Desipramine was continued for 7 weeks with no improvement, so it was stopped and fluoxetine, 20 mg/day, was started. Five days later, the patient became euphoric, very talkative, hyperactive, and grandiose. He complained of racing thoughts and stayed up all night. This behavior was observed for 2 days, and then lithium was started and fluoxetine discontinued. The patient responded within a few days. His manic symptoms improved, and he became euthymic. The patient was discharged and followed as an outpatient. Two months after discharge he was euthymic and doing well on a regimen of lithium, 300 mg t.i.d., and thiothixene, 5 mg h.s.

The mechanism of mania precipitated by antidepressants is not known, but it is believed to be principally related to an increase in the neurotransmitter norepinephrine and/or dopamine (4). In this case, the patient had a 7-week trial of the tricyclic desipramine with no "switching." He also continued to receive thiothixene, which would lower dopamine levels. The manic episode was precipitated 5 days after desipramine was discontinued and fluoxetine, which is known to have a selective serotonergic action (5), was started. Clinicians should be aware that fluoxetine may precipitate mania in adolescents and that "switching" may be precipitated by antidepressants with selective serotonergic action, such as fluoxetine.

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Distinguishing Borderline Patients With Splitting

SIR: No diagnostic category of mental illness provokes more confusion and debate among clinicians and researchers than borderline personality disorder (1). Some deny the validity of the notion altogether. Pointing to the extreme arbitrariness of the concept, George Vaillant remarked recently during a psy-

chiatry seminar, "One resident's borderline is another resident's wife."

Most of the *DSM-III-R* behavioral criteria for borderline personality disorder are consistent with the supposition of splitting. It is possible, however, to fulfill any five of the criteria required for this diagnosis *without* evidence of splitting.

As a clinician, I have seen many patients diagnosed as borderline who do not use the splitting defense, although otherwise their pathology is similar in presentation to that of patients who do. Bond (2) has reviewed two studies that attempted to determine whether patients diagnosed with borderline personality disorder use image-distorting defenses (splitting, projective identification, idealization-devaluation) to a greater degree than patients with other mental disorders. The first, using Bond's self-reporting Defense Style Questionnaire, showed no significant difference between the two groups; the second, using Perry and Cooper's Defense Mechanism Rating Scale, where clinicians rate videotaped interviews with patients, did show a significant difference.

It is clear that there is a discrepancy between *DSM-III-R*'s purely behavioral criteria for borderline personality disorder and the original psychodynamic formulation of the disorder, which takes splitting to be the core pathology (3, 4). I propose that borderline personality disorder be redefined so that patients who use the splitting defense are classified separately from patients who fulfill *DSM-III-R* criteria for borderline personality disorder but do not use that defense. The diagnosis for the former group could be called borderline personality disorder with splitting, and for the latter, borderline personality disorder with no splitting. Making this change would help rescue borderline personality disorder from being the "wastebasket" diagnosis that it is now and have significant consequences for treatment and research.

With this distinction, therapists treating patients known to split would be more likely to use techniques shown to be effective in integrating split-off fragments of the self and others (3, 4). Research into the nature and origin of borderline personality disorder, particularly efforts to uncover a possible neural concomitant for borderline splitting (5), would improve because the focus would be on a more homogeneous phenomenon. And "borderline" patients who do not split would benefit because different sources of their pathology could be considered and different treatments tried.

A distinction needs to be made between two common uses of the word "splitting." "Borderline splitting" is a descriptive term that specifies how borderline patients constitute their experience of self and others in fragments of alternating polarity (e.g., idealization-devaluation). It is undeniable that some borderline patients behave in this way. "Primitive splitting," on the other hand, defines a hypothetical defensive process carried out by an infant during the separation-individuation phase (18–36 months), which may or may not be responsible for later borderline splitting and borderline pathology.

It is the descriptive borderline splitting that I propose as the criterion for distinguishing the two types of borderline personality disorder. One can accept this concept with or without embracing the hypothetical notion of primitive splitting.

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Serum Iron and Neuroleptic Malignant Syndrome

SIR: T. White, M.B., Ch.B., and Keith Brown, M.B., Ch.B. (1) recently suggested that reduced serum iron may contribute to the pathophysiology of neuroleptic malignant syndrome through a mechanism of D₂ receptor hypofunction, a mechanism that they have postulated to underlie a relation between low serum iron and akathisia. In response to this suggestion, Patricia I. Rosebush, M.D., and Michael F. Mazurek, M.D. (2) observed that in a fraction of their cases of neuroleptic malignant syndrome, low serum iron levels did not precede the episode but occurred during the course of the syndrome and "are specific to the disorder itself." They speculated that in neuroleptic malignant syndrome, a sudden decrease of serum iron follows an as-yet unidentified initiating factor and may then contribute in some way to the clinical picture by interfering with D₂ receptor functioning.

Barton et al. (3) have confirmed the relation between iron deficiency and akathisia but point out that neuroleptics can lead to a redistribution of body iron, with accumulation in certain structures of the brain. According to these authors, this accumulation may lead to dopamine receptor supersensitivity and, when it occurs in the basal ganglia, to destruction of tissue. Thus, clinical manifestations of an interaction between iron deficiency and neuroleptic activity may be complex.

There is some evidence that low serum iron may make a specific contribution to the pathophysiology of neuroleptic malignant syndrome. In rats, diet-induced iron deficiency results in a blunting of the hypothermic response to *d*-amphetamine, and in this respect iron deficiency is similar to the action of neuroleptics (4). This effect appears to be mediated by D₂ receptors. Moreover, in both treated (*d*-amphetamine) and untreated animals, the normal circadian rhythm of thermoregulation and motor activity is reversed. Since the hypothalamus has been implicated by many (5) as the site of thermoregulatory dysfunction in neuroleptic malignant syndrome, it is interesting to note that the concentration of nonheme iron in this structure is very high (4), suggesting that adequate iron levels may be important for normal hypothalamic (i.e., thermoregulatory) function. Indirect support for a physiologic link between serum iron and thermoregulation is provided by the response to infection, in which both the drop in serum iron and the increase in body temperature that normally occur appear to be mediated by a common factor (6). The role of acute and chronic iron deficiency in the pathophysiology of neuroleptic malignant syndrome deserves further investigation.

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EEG Abnormalities Associated With Clozapine Treatment

SIR: Ellen Haller, M.D., and Renée L. Binder, M.D. (1) recently provided recommendations for the clinical management of clozapine-induced seizures. They suggested that any increase in the clozapine dose beyond 600 mg/day should be made only after an EEG has been read as normal. We wish to report our observations and comments on the EEG abnormalities associated with clozapine therapy.

We recorded EEGs, with the International 10-20 System, before and during clozapine treatment of 16 schizophrenic patients who had been treated with conventional neuroleptics for several years without effect. Daily clozapine doses varied from 300 mg to 700 mg (mean=512 mg/day). Three patients received a dose greater than 600 mg/day. On the basis of detailed medical histories and examinations, none of the patients was known to have had previous epileptic seizures or epileptiform EEG findings. Prior to the clozapine therapy, the EEGs of 11 patients (69%) were normal, and mild to moderate disturbance of background activity was seen in five patients (31%). During clozapine therapy (1-42 months from onset), all patients showed abnormal EEG findings. Twelve patients (75%) had profound disturbance of background activity and also paroxysmal episodes consisting of delta and theta waves. In seven patients (44%) these paroxysms were classified as epileptiform, consisting of spikes, polyspikes, or spike and slow wave complexes. Four patients (25%) had moderate disturbance of background activity with relatively abundant generalized theta activity. One patient (taking a daily clozapine dose of 500 mg) who had received ECT earlier, experienced seizures, which were controlled with carbamazepine therapy.

On the basis of our findings, it seems that most patients receiving clozapine treatment have abnormal EEGs. This agrees with an earlier study by Isermann and Haupt (2), who examined 36 patients receiving clozapine and found abnormal EEGs for 26 patients (72%). Sixty-four percent of the patients had paroxysmal episodes, 22% of which were classified as epileptiform discharges. It has been suggested that paroxysmal EEG abnormalities are associated with better clinical outcome; i.e., patients with such clozapine-induced EEG findings tend to have better response to clozapine therapy than patients whose EEGs remain normal (3, 4). It seems that clozapine in a therapeutic dosage may alter human EEGs in a more profound way than any other medication used nowadays. However, EEG data obtained from several hundred patients imply that there is no clear relation between the paroxysmal EEG activity caused by a psychoactive drug and the clinical appearance of seizures (4). We think that abnormal EEGs showing disturbance of background activity or nonepileptiform paroxysms should not contraindicate increase of the clozapine dose beyond 600 mg/day if no signs of clinical adverse effects are observed.

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Clozapine Concentrations and Clinical Response in Schizophrenic Patients

SIR: Paul J. Perry, Ph.D., and associates (1) have made a case for a threshold plasma clozapine level. However, their data show an even more robust measure of change; eight (89%) of nine of their patients who had Brief Psychiatric Rating Scale (BPRS) scores of 43 or less "improved" according to their criteria, whereas only three (15%) of 20 who had BPRS scores above 43 improved. It appears that the major criterion of success in these refractory patients was a less severe psychosis.

Of great interest was one of the patients who dropped out of the study, described as having fever, hypotension, and an elevated creatine phosphokinase level. Do Dr. Perry and associates consider this a case of neuroleptic malignant syndrome?

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Dr. Perry and Associates Reply

SIR: Dr. Jeffries is correct in stating that the baseline BPRS score was a major criterion of a successful response to clozapine in our patient group. However, this factor needs to be placed in its proper context by submitting this variable to multiple linear regression analysis.

Multiple regression analyses were completed by regressing the independent variables—baseline BPRS score and mean weekly clozapine and norclozapine plasma concentrations (ascertained during weeks 1, 2, 3, and 4)—against the dependent variable—BPRS score at week 4. An alpha level of 0.05 was considered significant. The multiple regression analysis revealed a statistically significant correlation only between the baseline BPRS score and the week 4 BPRS score ($p=0.0004$). However, a nonresponder with a mean steady-state clozapine concentration greater than 3 standard deviations above the mean was removed from the data set. With this outlier removed, the clozapine variable as well as the baseline BPRS variable reached significance ($p=0.03$). A one-tailed model was assumed in this analysis, since the data were assumed to change in a negative direction; i.e., as the week 4 BPRS score

decreased, the clozapine concentration increased. The norclozapine variable did not reach significance.

Concerning the patient who dropped out, we did consider this case an example of neuroleptic malignant syndrome. The case is described in detail elsewhere (1).

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Role of Psychoanalytic Thought in Twentieth-Century American Psychiatry

SIR: In his provocative overview of twentieth-century American psychiatry (1), Melvin Sabshin, M.D., offers an essentially negative interpretation of the role of psychoanalytic thought. For example, Dr. Sabshin accuses psychoanalysis of dealing a deathblow to nosology, ignoring epidemiologic research, shunning social and community psychiatry, shifting interest away from the treatment of the severely ill, failing to develop appropriately sophisticated theoretical models, promulgating ideology rather than empirical science, universalizing psychopathology and thus stigmatizing everyone with illness, and, finally, perpetrating all of the above with a "siege" mentality.

It is well-known that Freud was highly skeptical of the ways in which his American colleagues would use psychoanalysis, emphasizing thereby the distinction between a body of knowledge and its application. Dr. Sabshin, however, strongly implies that psychoanalysis per se is inherently at odds with the work of modern psychiatry—a point that warrants refutation.

I wish to stress the fact that psychoanalysis, being first and foremost a science of the unconscious, is in no way intrinsically opposed to psychiatry. Nosology, epidemiology, genetics, social psychiatry, etc. all have their rightful places within the edifice of psychoanalytic theory and its application to the treatment of mental disorders.

Nosology, in particular, has always been a prominent concern throughout the development of psychoanalysis, as a perusal of Fenichel's classic text (2) easily demonstrates. If psychoanalytic nosology has at times been conducted on deeper levels and in a more specific fashion than that offered by *DSM-III-R*, it is nosology nonetheless, and serves to complement the more superficially phenomenologic approach.

When Dr. Sabshin imputes a deleterious effect to the "universality of psychopathology" extant in Freud's work, he fails to acknowledge the profound humanistic revolution that Freud inaugurated. By demonstrating the universality of psychic mechanisms, Freud eliminated the sharp distinction between the normal and the pathological—a distinction that had hitherto led to the ostracism and persecution of the mentally ill. Freud's ideas in fact provided a tremendous impetus toward destigmatization of those suffering from emotional disorders, whether psychotic or neurotic.

Dr. Sabshin's charge that analysts "failed to perceive the enormous policy influence exerted by psychoanalytic theory and practice" (1, p. 1269) has an ominous ring. Does Dr. Sabshin mean to imply that scientific theory should be fash-

ioned to accord with so-called policy expectations and not with the empirical data of observation? Surely, an enterprise that seeks to mold its theories in accordance with political appeal or public acceptance does not deserve to be called a science.

Finally, Dr. Sabshin gives the unfortunate impression that he denies altogether the fundamentally empirical nature of psychoanalysis. It may be this attitude that explains why his scenario for the future fails to emphasize the absolutely crucial role played by a knowledge of the unconscious in establishing a truly scientific psychiatry.

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Comments on Projective Identification

SIR: Psychoanalytic concepts often need to be "translated" into simpler, phenomenological language in order to be useful to general psychiatry. The attempt by William N. Goldstein, M.D. (1) to clarify the highly complex and controversial notion of projective identification is therefore quite welcome. Another similar and equally good attempt was recently made by Ramchandani (2), although it was not mentioned by Dr. Goldstein in his article.

A more significant omission, however, involves the positive aspects of projective identification (3, 4). All of Dr. Goldstein's clinical examples involve the disowning and depositing into others of undesirable self representations riddled with anxiety, anger, inferiority, inadequacy, confusion, etc. In other words, the self representations that undergo projective identification involve attributes that are "undesirable" in a common-sense sort of way. While this holds true for the majority of cases, things are a bit more complex. To some patients, what appears undesirable (as a result of having internalized the dictates of a disturbed and cruel family of origin) involves their capacity for love, vigor, hope, authenticity, wit, playfulness, etc. Such patients deposit the endangered healthy aspect of themselves into the therapist, whom they then admire, value, and idealize. The therapist who is the recipient of such projective identification feels alert, active, vigorous, and hopeful for the patient's progress. While Dr. Goldstein is clearly not alone in overlooking such instances of positive projective identification, the omission does weaken his otherwise excellent article.

The importance of recognizing positive projective identification (4) lies in both diagnostic and therapeutic realms. For instance, narcissistic individuals frequently deposit their inferiority and shame-laden self representations into others, causing them to experience such feelings. Schizoid individuals, on the other hand, deposit their optimistic and sane attributes into others for safekeeping and thus mobilize hope, curiosity, and rescue fantasies in the latter. Therapeutically, too, such conceptualization has significance. In the treatment of a severely self-loathing individual, for instance, a constructive step is taken by the therapist in gradually familiarizing the patient with a benevolent view of him (5). This good image of the patient inside the therapist is the result not only of the therapist's kindness but also of the patient's use of positive projec-

tive identification. The patient discovers this image, feels it, tries it out, and eventually makes it his own.

In light of its diagnostic and therapeutic significance, the positive aspect of projective identification seems too important to be disregarded in a comprehensive review of the subject.

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SIR: I would like to thank Dr. Goldstein for his very clear, instructive, and useful review of projective identification (and projection). I have, over years of supervising psychiatric residents who are beginning to do psychotherapy, come upon some helpful ways of clarifying this sometimes vexing concept.

It seems to me that one of the central difficulties in understanding projective identification is that it seems so cumbersome. That is to say, what leads people to make use of a defensive system that seems (at least as described) so remarkably complicated? What are the people who use this defense attempting to accomplish?

I believe that it is essential to the understanding of the concept of projective identification to recognize that it is much more than a defense mechanism (i.e., an attempt to disavow a painful feeling or idea). Projective identification is reflective of the essential human need to communicate our distress to others. If one looks at human development, it is clear that our earliest communications are fueled by need. Infants, by virtue of their complete helplessness, can only achieve gratification through communicating their distress. This state of affairs continues, to one degree or another, throughout childhood. The changes that ideally occur as the child becomes more independent and differentiated are 1) development of the ability to express need and distress more effectively in a verbal way and 2) a greater sense of being able to tolerate discomfort, delay gratification, and master one's impulses on the basis of the conviction that relief in some form will ultimately come. These changes, of course, depend at least partly on the parents' teaching the child to name and express his or her feelings, the parents' willingness to listen to what the child has to say, and, finally, a relatively consistent, predictable response to the child (this doesn't necessarily mean always gratifying, but maintaining an acceptable ratio of gratification to frustration and teaching the child to find gratification symbolically).

As we reach adulthood, this need to communicate distress is still very powerful (indeed, this is what leads psychotherapy patients to enter a stranger's office and communicate important personal information). When the conditions I have noted are not met, the person is left with nonverbal, primitive means of communication. The striking lesson of projective identifica-

tion is that it has sensitized us to the uncanny ability of people to communicate their feelings indirectly, nonverbally, but in very powerful ways, and shown us that people can learn and develop by watching others grapple with their distress. A frustrated, angry child who has provoked his or her parent to feel frustrated and angry will learn from the parent's handling of the situation.

Keeping this in mind also helps to clarify the work in therapy with patients whose primary mode of affective communication is through projective identification. That is, the therapist needs to help fulfill the tasks I have listed. The patient must be helped to use language to communicate inner experience and be shown that impulses and needs can be contained, symbolized, and, one hopes, appropriately gratified once they can be talked about.

VICTOR SCHWARTZ, M.D.
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SIR: Dr. Goldstein's article on projective identification is timely and useful. 1) It clarifies some definition of the concept. 2) By presenting six case vignettes, it gives the clinician some substance to "chew on" while reacting to the content. And therefore 3) it gives the clinician an opportunity to respond cogently to the content. I wish to make the following observations.

In case 2, the question arises, Did the analyst feel overwhelmed, since he expected to be effective in the patient's change, and as the events turned out, his own expectations regarding change were not met?

In case 3, Dr. E, according to her behavior, had a self-image of exaggerated importance and superiority. She used demeaning of Dr. F as a way of enhancing that image (certainly a well-known personality trait). Dr. F, lacking self-confidence in dealing with a superior, had difficulty in coping with the demeaning ways of Dr. E. Was this identification, or was Dr. F's behavior an expression of personality trait in interaction with another individual?

In case 4, the therapist's inability to reach the patient and have an effect on him could have resulted in her feeling impotent, "destroyed," and overwhelmed. This again requires knowledge of the therapist's expectations at that moment in the doctor-patient relationship. Was identification the dynamic?

In case 5, Mr. H had a personality trait of seeing himself as superior, especially in the area of maintaining control of anxiety. Additionally, he needed to maintain a detached type of relatedness. He therefore demeaned others who had expressive anxiety. Since he had a girlfriend who was highly vulnerable to any type of thought connected with anxiety, she was vulnerable to his half-truths. Her reactions stemmed from her own hypersensitivity to apparent danger rather than from identification. Meanwhile, Mr. H maintained his sense of superiority and detachment in the interpersonal interaction.

In case 6, during the specific session discussed, the therapist closely followed the patient's expression as well as its intensity. The patient was like a yo-yo, and in following his gyrations there could have been a sense of disorganization and the possibility of a rupture, i.e., the end of the doctor-patient relationship. The psychiatrist had to collect her thoughts. But meanwhile, is it not possible that anxiety feelings were engendered at the thought of losing the patient? Again, the reactions were the expressions of the individual's traits in interaction with each other, which expressed the anxiety.

Dr. Goldstein has emphasized the importance of the inter-

personal interaction. The clinical findings in his case vignettes can be understood in terms of the interaction. The interaction has a specific meaning to each of the persons involved. Each brings his or her requirements to that moment. The combination of meaning and the expectations can result in feelings of anxiety and being overwhelmed and destroyed.

LEONARD M. GOLD, M.D.
Stamford, Conn.

SIR: In his timely and erudite clarification of projective identification, Dr. Goldstein points out that much of the controversy about the concept stems from the difficulty in differentiating projection from projective identification. Kernberg (1) believes that projection is a more sophisticated defense mechanism associated with repression in higher-level character disorders. Dr. Goldstein appears to echo that view when he says that projection occurs in a setting of clearly differentiated ego boundaries. I believe that projection is being unfortunately used by these writers interchangeably with the mechanisms of externalization and displacement.

The answer to the dilemma may lie in Kernberg's earlier work on internalized object relations (2). As a result of incomplete differentiation of self images from object images in psychotic patients, there is regressive fusion of self and object images, leading to a blurring between self and nonself. In borderline patients, the defect lies in the next step, i.e., incomplete integration of "good" and "bad" self and object images, leading to an intensification and pathological fixation of splitting processes.

Projection is the logical primary defense mechanism in psychotic conditions in which transfer of mental content from a self representation to an object representation would occur with ease. The break with reality is complete. There is no need for an ongoing relationship with the object because the object ceases to exist. In "high-level" character disorders, there is predominance of displacement, in which mental content is transferred from one object representation to another, or externalization, in which an internal conflict is repressed and experienced in one's capacity as a member of a group rather than at a personal level, as in pervasive racism or antisemitism.

In borderline patients (1), when a transfer of the mental content of an unwanted self representation occurs in the corresponding "bad" object representation, complete merging between self and object images is prevented by the continued operation of splitting. The preservation of "good" self and object representations prevents a complete breakdown of object relatedness. Instead, a hide-and-seek relationship develops and persists between partially blurred self and object representations, which spills over into the interpersonal realm.

Thus, projection really may be a more primitively complete defense mechanism than projective identification, which, in turn, is more primitive than defenses such as externalization and displacement. It is difficult indeed to discern in some of Dr. Goldstein's examples where countertransference ends and projective identification begins. This is particularly so in patients who use displacement rather than projection in step 1. It also seems to me that Porder (3) erroneously equates projective identification with "repetition compulsion," albeit in a therapeutic setting.

That the stage of interpersonal enactment forms such an essential core of projective identification is a reflection of the nature of borderline pathology, which plays itself out in vulnerable interpersonal settings. The stage of reinternalization should really be seen as a sequel to the defense proper. In

uncontrolled situations, it leads to the development of pathological conditions, e.g., sadomasochistic relationships and forms of erotomania (4).

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Dr. Goldstein Replies

SIR: All of these letters contribute valuable additions to my article on projective identification. Regarding Dr. Akhtar's letter, I agree with him about my omission of the concept of positive projective identification. As referenced by Dr. Akhtar, the work of Hamilton (1, 2) distinguishing between positive and negative projective identification is particularly relevant here. Hamilton believes that the concept of positive projective identification is especially valuable in working with psychotic patients. He provides interesting examples in which psychotic patients project grandiose positive aspects of themselves onto the therapist and also examples in which therapists project positive attributes of themselves onto psychotic patients who lack these qualities.

Unlike Hamilton, in referring to positive projective identification, Dr. Akhtar emphasizes the projection of "undesirable" positive aspects of oneself. I find Dr. Akhtar's distinction between narcissistic individuals who use negative projective identification and schizoid and self-loathing individuals who use positive projective identification quite interesting and useful. I certainly agree with Dr. Akhtar's ideas about the psychotherapeutic use of positive projective identification.

Regarding Dr. Schwartz's letter, I think he is addressing a crucial question regarding projective identification; that is, what types of people use this mechanism on a regular basis? Dr. Schwartz feels that projective identification is a primitive means of communicating distress, used by people who are more comfortable expressing themselves in actions than in words. These are people, according to Dr. Schwartz, who have had difficulty in learning how to tolerate discomfort, learning how to delay, mastering their impulses, and learning how to relate on a verbal level. I think Dr. Schwartz's comments are highly relevant, clearly complementing Porder's ideas (3). Porder notes that people who typically use projective identification are sicker individuals who have difficulty expressing their conflicts verbally. Porder believes that these individuals often grow up with disturbed and aggressive parents, by whom they are victimized and with whom they identify.

Regarding Dr. Gold's letter, I agree with him that the interpersonal interaction should be understood in terms of both the projector and the recipient of the projection. The conflicts, sensitivities, and vulnerabilities of the recipient are highly relevant here; in fact, they are crucial in determining to what extent the projection is accepted. However, I think that Dr. Gold deemphasizes the aggressive, forceful, coercive, and some-

times attacking posture of the projector. I feel it is this posture that is largely responsible for the feelings occurring in the recipient.

Regarding Dr. Ramchandani's letter, I feel that the main problem in understanding projective identification involves definition. The term is used in too many different ways. To a lesser extent the same problem applies to the terms "projection" and "externalization." If everyone agreed on the definitions of key terms, there would be much less confusion related to projective identification.

Dr. Ramchandani's idea that projection is a more primitive response than projective identification should be carefully considered. Hamilton (1) has made the same point, citing both theoretical and clinical evidence. In projection proper there is a clear loss of reality testing, as demonstrated by a conviction that an aspect of the self is in another person. In projective identification, the loss of reality testing is not total, as some lack of clarity remains about the location of the self representation. This, of course, applies to projections of self representations only. Clinically, projection proper is most characteristic of severely disturbed psychotic patients, whereas projective identification is more characteristic of less disturbed borderline patients. Despite my article, which might have conveyed a different impression, I agree with Dr. Ramchandani and Dr. Hamilton.

Regarding projective identification and countertransference, I feel that countertransference begins to operate when the therapist begins to respond (usually unconsciously) to the projection. With this in mind, some of the examples involve countertransference phenomena.

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Research on Alcohol Abuse

SIR: I enjoyed reading the report "The Natural History of Alcohol Abuse: Implications for Definitions of Alcohol Use Disorders" by Deborah S. Hasin, Ph.D., and associates (1). This type of research is extremely necessary in order for us to assess better what we do as clinicians and to improve patient care. However, the study's results do not include essential outcome variables. Most important is the lack of information about abstinence (both current and total) in the "remission" group since the initial assessment and prior to the follow-up. Since 47% of the initial 71 abusers and 39% of the initial 109 dependent drinkers were classified at follow-up as being in remission, significant percentages of patients at follow-up were not well described. Babor et al. (2) and Vaillant (3) have emphasized the importance of measuring abstinence as part of alcohol dependence/abuse follow-up.

The second concern focuses on the statistical analysis. The authors reported that the difference in outcome between abusers and dependent individuals was statistically significant at the $p < 0.05$ level ($\chi^2 = 4.12$, $df = 1$). This referred to the difference in percentages of patients assessed as dependent at follow-up when comparing those initially identified as abusers and those

initially identified as dependent. Information about abstinence status would be important here, since for many patients abstinence is the only alternative to serious problems, whether they are described as due to dependence or to abuse. A difference in abstinence as the type of remission might have strengthened the authors' case.

When the percentages of patients on each of the three outcome measures (dependence, abuse, and remission) are compared between those originally considered to have been dependent and those originally considered to have been abusers, there is no statistical difference in outcome ($\chi^2 = 5.41$, $df = 2$, $p > 0.05$). Moreover, if the abuse and dependence categories are combined, the percentage of patients who are still having problems at follow-up is 53% for the initial abusers and 61% for the initially dependent individuals. These differences are not statistically significant.

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P. JOSEPH FRAWLEY, M.D.
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Dr. Hasin and Associates Reply

SIR: In our article we focused specifically on indicators of DSM-III-R alcohol abuse and dependence at initial assessment and follow-up. According to DSM-III-R, individuals may be in full remission from alcohol dependence whether drinking or not, as long as they no longer show symptoms of the disorder. We agree with Dr. Frawley that investigation of the relation of alcohol consumption to alcohol-related symptoms is important, but that issue goes beyond the scope of our article.

In an earlier version of this report we classified the entire cohort of 593 men into four groups at initial assessment and then examined their status with regard to these four classifications at follow-up. We changed to the published groupings because the original classifications did not lend themselves to a joint statistical test that addressed our major point of interest. However, we feel that these original groupings defined clinically meaningful differences in status, offer additional information to the interested reader, and also clarify our interpretation of the results. Group 1 included men without abuse or dependence indicators, as described in our earlier letter (1). Group 2 included men with abuse indicators only, as reported in the article. Group 3 included men with both abuse and dependence indicators ($N = 69$), corresponding to the combinations of problems most often seen in alcoholism treatment facilities. Group 4 included men with dependence indicators and no abuse indicators ($N = 40$).

Four years later, 46% of group 2 and 23% of group 3 were in remission, 24% of group 2 and 20% of group 3 had abuse indicators only, 21% of group 2 and 42% of group 3 had indicators of abuse and dependence, and 8% of group 2 and 14% of group 3 had dependence indicators only. The outcome of group 4 was 68% in remission, 5% with abuse only, 18% with both abuse and dependence indicators, and 10% with

dependence only. In our view, the meaning of the findings for group 4 is not entirely clear and needs further study with larger samples. In a number of ways, the comparisons between groups 2 and 3 seem most directly related to our question about differences in the history of abuse and dependence. If we conduct a test of the differences in outcome between these two groups (using the four classifications), the results are $\chi^2=11.62$, $df=3$, $p<0.009$. We hope that this additional information helps address the concerns of Dr. Frawley and others.

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Fatal Hyperthermia Syndrome

SIR: The article by S.J. Kish, Ph.D., and associates (1) presents important neurochemical findings and advances the field in suggesting use of "fatal hyperthermia syndrome" to replace "lethal catatonia" and "neuroleptic malignant syndrome." The field would be even better served, however, by the term "hyperthermic catatonia."

"Neuroleptic malignant syndrome" is misleading in that the syndrome had been reported in the medical literature for more than a hundred years before the availability of neuroleptics (2), it has been reported to result from withdrawal of L-dopa in patients not taking neuroleptics (3), and it is not always fatal (4). "Lethal catatonia" is also misleading with respect to prognosis: some patients have recovered without any specific medical treatment (2). "Fatal hyperthermia syndrome" is also misleading for implying that the condition is always fatal and for implying that there is a consensus on what constitutes the "syndrome."

"Hyperthermic catatonia" avoids all these misrepresentations and avoids premature etiological and prognostic closure.

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ROGER PEELE, M.D.
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SIR: I hope and expect that you will get many letters in regard to the article on brain neurotransmitter changes in three patients with fatal hyperthermia syndrome. On the basis of what we know already of the relation between neuroleptic medications and the fatal hyperthermia syndrome, it is hard not to

come to the conclusion that in each of the cases described in the article, the cause of death was the continued treatment with neuroleptic medications despite early signs of neuroleptic malignant syndrome. I find it surprising that the patients would be treated in such a manner, but it is even more surprising that there was no discussion in the article of the effect of the treatment on the patients' outcome. This glaring omission renders suspect any conclusions that might be drawn by the authors.

JAMES G. SEYMOUR, M.D.
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SIR: Dr. Kish and associates reviewed autopsy findings in three cases of "fatal hyperthermia syndrome." Cases 1 and 2 were diagnosed as "fatal catatonia" and case 3 as neuroleptic malignant syndrome. We believe that all three cases were instances of neuroleptic malignant syndrome, because in each one the hyperthermia followed the administration of a neuroleptic. Moreover, although catatonic features (particularly stupor) were a predominant manifestation of the illness in cases 1 and 2, there is a suggestion from the brief clinical reports provided that before neuroleptics were given, both of these patients showed possible catatonic signs: restlessness (catatonic excitement?) and depression (catatonic stupor/mutism?) in case 1 and restlessness and "loss of contact with surroundings" in case 2. In both cases the onset of the initial illness was sudden.

We recently described (1) a series of five consecutive cases of neuroleptic malignant syndrome in which an acute catatonic state (based on *DSM-III-R* criteria, namely, stupor/mutism alternating with excitement) preceded the development of the syndrome. In each patient the neuroleptic malignant syndrome was precipitated within 72 hours of the administration of a parenteral neuroleptic agent (never more than three doses, and in two cases only one dose). The temperatures recorded in our patients were high, but not as high as those reported by Dr. Kish and associates. All of the patients recovered after immediate discontinuation of the neuroleptic and with supportive treatment (the use of dantrolene and dopaminergic agonists was not necessary).

We hypothesized (1) that the prodromal catatonia was associated with low brain dopaminergic activity, which was further decreased by the subsequent administration of a neuroleptic, thereby culminating in the neuroleptic malignant syndrome. This hypothesis gains support from the findings of Dr. Kish and associates and from other workers who have demonstrated a reduced functional activity of the brain dopamine system during neuroleptic malignant syndrome and possibly even before the emergence of the illness. Furthermore, it is noteworthy that schizophrenia is a relatively rare antecedent diagnosis of patients with neuroleptic malignant syndrome (2). We propose that the hyperdopaminergic state postulated to occur in schizophrenia (or certain forms of it) protects patients from neuroleptic malignant syndrome.

We therefore emphasize the potential hazard of using neuroleptics (in even a single dose) in patients showing features of catatonia. Certain clinical signs such as stupor/mutism alternating with agitation (the latter has been observed to be a frequent precursor of neuroleptic malignant syndrome [2, 3]) are risk factors for the onset of neuroleptic malignant syndrome. Clinicians should carefully evaluate whether such behavior falls into the catatonic spectrum before administering neuroleptics. Where catatonia is suspected, we would recommend the use of benzodiazepines, which appear to have some efficacy in the management of catatonic states (4).

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Dr. Kish and Associates Reply

SIR: We thank Dr. Peele for his attention to our article and welcome his suggestion of a possible replacement for the name of the medical condition that we described as the fatal hyperthermia syndrome. We proposed "fatal hyperthermia syndrome" as a short, "neutral" term that would be generally descriptive for patients with either fatal catatonia or neuroleptic malignant syndrome. Although both fatal catatonia and neuroleptic malignant syndrome are often fatal conditions, we agree that the modifier "fatal" could be deleted, since patients with either condition can recover without medical treatment. We also would be in favor of the addition of "catatonia" to the name of this condition, which describes clinical aspects of both fatal catatonia and neuroleptic malignant syndrome. Whichever term is finally selected by the psychiatric community, we strongly agree with Dr. Peele that it must avoid any "premature etiological and prognostic closure."

In his letter Dr. Seymour suggests that the cause of death in each of the cases we examined was the continued treatment with neuroleptic drugs. In our article we pointed out that of the three cases studied, one patient, with a history of chronic schizophrenia (case 3), had received a clinical diagnosis of neuroleptic malignant syndrome; in this case neuroleptic treatment was immediately discontinued and replaced with dopaminergic (carbidopa/l-dopa) medication. On the other hand, we also clearly stated throughout the text of our article that the other two acutely psychotic patients (cases 1 and 2) were diagnosed at admission to the hospital as having Stauder's "fatal" or "lethal" catatonia syndrome (described in the literature, as pointed out by Dr. Peele, well before the advent of neuroleptic drugs) on the basis of the classic signs of this condition (severe psychomotor agitation followed by catatonic stupor and terminal hyperthermia; age range, 18-to 26 years [1]). These patients were treated with neuroleptic drugs and ECT, which have been found in some studies to be beneficial (1, 2). As recently discussed in the *Journal* by Castillo et al. (1), clinical differentiation between life-threatening fatal catatonia and the equally life-threatening neuroleptic malignant syndrome may be critical, since the former condition may actually be improved by neuroleptic drugs, whereas in the latter, neuroleptic medication should be discontinued.

On the other hand, as Dr. Robins and Dr. White write, their clinical study apparently indicates that some patients presenting with the classic features of fatal catatonia and receiving neuroleptic treatment improve upon discontinuation of the neuroleptic drug. This suggests that neuroleptic drugs may precipitate a hyperthermia syndrome in any predisposed patient, regardless of his or her primary clinical condition. Our neurochemical observations suggesting an underlying brain

dopaminergic disturbance in patients who had been clinically diagnosed as having fatal catatonia (cases 1 and 2) actually allow for an aggravating effect of the brain dopamine receptor blocking neuroleptics; in such cases discontinuation of neuroleptic medication would be indicated, as pointed out by Dr. Robins and Dr. White. However, our neurochemical data indicating a primary brain dopaminergic disturbance would also strongly imply that use of neuroleptic drugs is not an obligatory requirement for the clinical expression of catatonia-hyperthermia syndrome, which, consequently, may have a lethal outcome regardless of whether neuroleptics are administered or withdrawn.

The obvious clinical dilemma regarding the appropriate treatment of patients having a (fatal) catatonia-hyperthermia syndrome can only be resolved by knowledge of the underlying brain (morphologic/neurochemical) mechanisms. It was the aim of our study to contribute to this goal.

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Comment on Analysis of Psychiatric Comorbidity in Twins

SIR: I read with great interest the article by Sverre Torgersen, Dr. Philos., on the comorbidity of major depression and anxiety disorders in twin pairs (1). The study of twins is a powerful tool for analyzing the basis of psychiatric comorbidity, where phenotypes are most often qualitatively defined. Depending on the problem one wishes to address, there are a variety of analytical techniques available (2, 3). The purpose of this commentary is to elaborate briefly on some of the conclusions suggested by Dr. Torgersen's data.

In psychiatry comorbidity can be due to a variety of mechanisms. It may reflect the variable expressivity of a particular gene or genes; the expression of closely linked genes, each independently responsible for one or the other disorder; disorders secondary to the primary disorder; or artifacts due to sampling methods, among other possibilities. There is currently some debate on whether a distinct form of depression with anxiety exists and the manner in which such a disorder is related to pure anxiety or pure depression. With reference to this issue, it is noteworthy that in the Torgersen data, the monozygotic and dizygotic co-twin rates for mixed anxiety-depression in twin pairs selected through probands with both

anxiety and depression were essentially zero. While a consistent association between anxiety and depression may not be robust across psychiatric samples, it is not unreasonable to suspect the existence of a biological subtype in which having both disorders represents a unique syndrome in a subset of individuals. Dr. Torgersen's data suggest that such a subtype may not exist, and in fact, mixed anxiety-depressive disorders may simply be a different expression of a liability toward depressive illness. It is surprising, however, just how small the twin concordances were for mixed anxiety-depression, because the two disorders should occur together to some extent by chance alone, given their independent base rates and heritabilities. The small sample size may account for this deviation.

Dr. Torgersen did not present clear data that address the possibility that anxiety may be associated with depression in his sample overall, although the data he did present suggest that the two disorders commonly co-occur. Such an association could be examined by ascertaining the frequency with which anxiety disorders are present in depressed versus psychiatrically unaffected subjects. A genetic basis for this association could then be studied by observing the relative magnitude of monozygotic and dizygotic cross-concordances for depression and anxiety across the entire sample of twins (e.g., examination of the rates of anxiety in co-twins of probands with pure and mixed depression combined).

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Dr. Torgersen Replies

SIR: Dr. Gilger stresses in his comments on my article the unique possibility for twin research to reveal the basis for comorbidity of psychiatric disorders. Comorbidity between disorder A and disorder B may be interpreted in at least five ways:

1. The mixed cases may be the typical disorder and the pure cases deviations from the core disorder.
2. The mixed cases may belong to disorder A, with disorder B being another disorder.
3. The mixed cases may belong to disorder B, with disorder A being another disorder.
4. The mixed cases may be partly an atypical or wrongly diagnosed disorder A, partly disorder B.
5. The mixed cases may be a specific disorder, different from both disorder A and disorder B.

Twin studies, however, can only give arguments for or against these hypotheses on an etiological basis, while treatment studies and follow-up studies may give other conclusions. And generally, as Kendler (1) has maintained, scientific data can never fully solve such nosological problems. Some of us are "lumpers" and like to think that all or nearly all disorders are basically the same disorder. Hypothesis 1 is their favorite. Others have a preference for separating syndromes;

they are "splitters" and like hypothesis 5. Both kinds of people are able to tolerate the other three hypotheses.

How should one analyze data on twins? Dr. Gilger is surprised how small the twin concordance is for mixed anxiety-depression. I am also surprised. He gives a reasonable explanation himself, namely, the small sample size. Only by replication through more twin studies may we reach firm conclusions.

Dr. Gilger misses "data that address the possibility that anxiety may be associated with depression in his sample overall." My article contains data on all my anxiety and depression index twins. Very few co-twins of twins with other disorders had anxiety or depression, so this would not help us in our analysis of the data. He asks for "the frequency with which anxiety disorders were present in depressed versus psychiatrically unaffected subjects." Anxiety disorders were never present in "psychiatrically unaffected subjects," because then they would have been affected!

Dr. Gilger suggests looking at "the rates of anxiety in co-twins of probands with pure and mixed depression combined" and comparing monozygotic and dizygotic twins. This is easily done from the data in my table 1. The monozygotic concordance for anxiety is 18% and the dizygotic concordance 14%, suggesting little genetic association between anxiety and depression when analyzed in this way. To combine pure and mixed cases would blur the relations between pure anxiety, pure depression, and mixed cases.

The relation between the mixed disorder and pure anxiety and depression is far from settled. The unfavorable outcome of mixed cases is well-known. Studies also show that individuals with mixed cases report poor parental bonding in childhood (2) and that they frequently have severe personality disorders in addition (3). In fact, pure cases of anxiety and depression do show more similarity in these respects than the pure and mixed cases.

Perhaps the mixed cases have some liability in common with the pure cases, at least with depression. Perhaps they have some unique liability in addition. Maybe both lumpers and splitters are right! A nosological system may be considered as a more or less successful delineation of cases that are the product of partly similar, partly different etiological processes. Twin studies may make a certain contribution to the disentangling of these processes.

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SVENN TORGERSEN, PH.D.
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Is Life a Wisconsin Card Sorting Test?

SIR: Alan S. Bellack, Ph.D., and associates presented a carefully executed study involving an application of the Wisconsin Card Sorting Test for patients with schizophrenia (1). They found that with appropriate cognitive instruction, their schizophrenic patients' test performance was remediable. The compelling question remains, of course, what all this has to do with real life from a clinical/rehabilitative perspective.

Indeed, the Wisconsin Card Sorting Test confronts individuals with a somewhat ambiguous challenge that approximates life in several interesting respects. The basic card sorting dilemma is that the rules of the game keep changing. Moreover, the individual has to figure out for himself 1) that the rule is subject to change, 2) when the rule has actually changed, and 3) what the new rule is. Thus, even if one is able to figure out the appropriate parameter in a particular situation, that parameter will soon be altered, and continued responses in the original format will now be "errors."

As a clinical/behavioral example, when a person enters a room, the first rules concern the way one interacts with people upon first encountering them. But then, after the initial encounter, the rules immediately change. One is no longer in the process of entering the group; one is now within the group, and rules of continuing acceptable behavior are different. In the ongoing social process, encounter rules continue to change rapidly as people cooperate, flirt, compete, seek support, etc. Moreover, contextual rules vary within each dyad depending on how well the other person is known, the circumstances of previous encounters, what else is going on, how many others are present, and so on. An individual who lacks the ability to recognize and adjust to each newly emergent set of rules, and instead perseverates with a previous behavioral set, is at a distinct disadvantage. Such an individual will not "fit" and will be repeatedly forced out. Ultimately, this individual may learn to avoid social encounters altogether.

Such a plight is distinctly reminiscent of the picture presented by many patients with schizophrenia. While current approaches to social rehabilitation in schizophrenia often focus on areas of discrete skill building (2), they generally do not attend to set change, i.e., improving abilities to recognize rule changes and adapt to them. The article by Dr. Bellack and associates raises an interesting possibility: that the ability to recognize and adapt to set changes is a capacity which can be taught, through appropriate techniques, even when the disorder which occasioned the deficit in that function might have a demonstrable neuropsychological basis. Although extrapolation to a vastly complex realm such as social interaction is necessarily an iffy proposition, and a number of crucial intermediate steps would be required, this proposition represents a testable hypothesis that has potential conceptual ramifications for rehabilitative strategies in this population. Only further examination and careful trials, of course, will properly elucidate whether this strategy has a generalizable usefulness.

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SAMUEL G. SIRIS, M.D.
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Dr. Bellack and Associates Reply

SIR: Dr. Siris has raised a number of important issues in his letter. There has been a marked discontinuity between laboratory studies of cognition and information processing in schizophrenia and the structure and focus of psychosocial interventions. The tenuous status of our treatment armamentarium may be ascribed in good part to excessive reliance on

clinical intuition and failure to consider basic research adequately in designing interventions. Thus, we agree with Dr. Siris's admonition that the functional and clinical applications of our results need to be examined. In fact, the stimulus for our Wisconsin Card Sorting Test study was the tacit implication that schizophrenic patients could not learn to reason or solve simple problems. While our study did not test the limits of their capability, the data certainly indicate that their impairment is at least partially remediable and that rehabilitation is a viable goal.

We share Dr. Siris's general optimism about the prospects for improving social competence, but we also urge caution. Knowledge of social rules and mores is a basic aspect of social intelligence, which is essential for effective social performance, and there is ample evidence that schizophrenic patients have deficits in this area. But social intelligence is just one part of the puzzle. Effective social performance also depends on the ability to detect and evaluate relevant social cues (i.e., social perception) and the ability to perform requisite social behaviors (i.e., social skill). Schizophrenic patients have repeatedly been shown to have marked deficits in both social perception and social skill (1). The training technology used in our study has a proven efficacy in remediating social skill deficits but has not yet proved to be effective in improving social judgment and the ability to solve social problems (2). Remediation of these complex information-processing skills will probably require a different type of intervention, which has yet to be developed. It also remains to be determined whether we can *remediate* information-processing impairments, as opposed to teaching compensatory strategies.

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Religious Issues in Psychiatry

SIR: Reading the recent article by Marc Galanter, M.D., and associates on the impact of evangelical belief on clinical practice (1), I verified once more that religion is an important sociocultural covariable that must be included in clinical and epidemiologic surveys. Larson et al. (2) reviewed four major psychiatric journals and found that only 3% of the quantitative studies included religious affiliation as a covariable.

In a recent study (3), I reviewed the first 300 consecutive admissions to the 12-bed psychiatric inpatient unit of a university general hospital in southeast Brazil. Our unit is a public facility that receives patients predominantly from the lower social class. The patients (166 female, 134 male) had a mean±SD age of 34.0±14.6 years. The most frequent diagnostic categories included neurosis and personality disorders (25.5%), affective disorders (24.2%), and schizophrenia (23.2%). All psychiatrists involved in this study and in the care of the patients were agnostics or atheists.

The objective was to verify to what extent 12 clinical and

sociodemographic variables could predict length of stay in the hospital. The mean±SD length of stay for the whole patient group was 19.4±18.7 days. Clinical diagnosis (patients with major disorders staying longer, $p<0.05$) and religious affiliation (Pentecostals staying a shorter time than Catholics, $p<0.05$) correlated significantly with length of stay.

What appeared especially surprising to me was that in our sample, Pentecostal patients were diagnosed predominantly as having schizophrenia, bipolar illness, or major depression—diagnostic groups which, however, predicted a longer stay for the whole sample. Why did Pentecostal affiliation predict a shorter stay? Brazil is a predominantly Catholic country (about 80%). From the 1950s until now, new evangelical churches, especially the Pentecostal ones, have shown a tremendous increase, from 1%–2% to more than 10% of the whole population. These sects, originating in the United States, have expanded dramatically in Latin America. Most of them are fundamentalist, with strict moral rules and emotionally intense rituals. Exorcism and faith healing are frequent practices. In comparison to Catholics, they have a more intense religious practice, stronger social control, and probably closer social support for members. Until now, to our knowledge, the mental health implications of this process have not been systematically studied. It is not unlikely that these groups may function as a stronger social network and thus contribute to the shorter hospital stay of their members.

The International Pilot Study of Schizophrenia (4) showed that schizophrenic patients in developing countries have a better outcome, in spite of material poverty and fewer and worse psychiatric facilities. Unfortunately, religious affiliation was not included in that study. Verghese et al. (5), in a controlled study in India, using the same instruments as the International Pilot Study of Schizophrenia but including religious intensity, found increased religious activities to be a protective factor in the outcome of schizophrenia. Albeit descriptive, our data support the importance of including religious affiliation and intensity as a covariable in mental health studies.

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PAULO DALGALARRONDO, M.D.
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Dr. Galanter and Dr. Larson Reply

SIR: Dr. Dalgalarrrondo presents interesting findings regarding shorter stays of Pentecostal patients hospitalized in Brazil, perhaps due to their intense and supportive religious affilia-

tion. His hypothesis that such religious experience can sometimes yield more rapid remission of acute mental illness is compatible with our own findings.

Attention to the impact of intense, religiously grounded experience on mental and physical functioning goes back, of course, to the classic work of Walter Cannon on voodoo death—in that case, negative impact. Striking positive and negative effects have been reported as well in religious and quasi-religious settings, from Erhard Seminars Training (est) (1, 2) to contemporary religious cults (3). Additionally, movements that are more secular in orientation but nonetheless carry religious connotations, such as Alcoholics Anonymous, clearly have an effect on recovery from addictive illness.

What is striking in its absence in the past is support for investigation of issues related to intense group influence and religion and their relation to organized therapeutic settings (4). Benefit could be derived from studies on this issue; ideally, they should be done with good controls but without losing access to the intense and mutative quality of zealous religious experience.

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Serotonergic Antidepressants and Obsessive-Compulsive Disorder

SIR: We read with interest the article by Michael A. Jenike, M.D., and associates (1) describing the results of their randomized, placebo-controlled trial of fluvoxamine in 38 patients with primary obsessive-compulsive disorder, which suggested that fluvoxamine was efficacious. We have some points to make concerning the authors' interesting hypothesis that the selectivity of the serotonergic activity (i.e., inhibition of serotonin reuptake) of the serotonergic antidepressants is inversely related to their clinical efficacy in the treatment of obsessive-compulsive disorder.

This hypothesis was based on the results of studies of several antidepressants, with differing pharmacological activity, that have been tested for use in the treatment of obsessive-compulsive disorder, i.e., fluvoxamine (1), clomipramine (2), fluoxetine (3), and sertraline (4). This difference in activity is characterized by the specificity and extent of the inhibition of serotonin reuptake by each drug. To support their hypothesis, the authors presented a table indicating the "relative potency" for the ex vivo inhibition of serotonin reuptake, the "relative selectivity" of this inhibition in comparison to the inhibition of norepinephrine reuptake, and the "effect size."

One crucial point in their discussion is the pertinence of the values for the effect size for each drug. Although the authors used the term "meta-analysis," this was apparently not per-

formed, since results from similar studies with the same drug were not pooled. The authors simply reanalyzed the data from their own studies (one for each product) without attempting to combine their data with those from other studies.

Furthermore, the authors compared effect sizes that are not strictly comparable, since three of the studies were placebo-controlled and one was uncontrolled. Therefore, it would have been more reasonable to consider only the controlled studies, especially since the effect size cannot be accurately assessed in uncontrolled trials. Instead, the authors, in the placebo-controlled studies, only considered data from patients who had received active treatment, which is equivalent to converting each of these to uncontrolled studies and ignoring the influence of nondrug factors (e.g., placebo response, psychotherapeutic effects, study effect) on the effect size. This leads to a biased estimate of the effect size, resulting in an overestimation of the "true" value and giving very misleading results, since this influence is not identical for all studies.

Therefore, it would be more meaningful if the authors were to recalculate a confidence interval for the mean effect size against placebo for the three products that were tested in double-blind, placebo-controlled studies in their research unit. This effect size could be the mean difference between the active product and placebo, the mean difference between before and after treatment, or the difference between the mean percentage decrease for active product and placebo. Readers could thus judge for themselves whether the confidence intervals are commensurate or not, even if this is not a direct statistical comparison.

The small number of trials used by the authors leads to another major limitation: selection bias, since the trials are included because the results fit the hypothesis.

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DR. P. CIALDELLA
PROF. J.-P. BOISSEL
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Dr. Baer and Dr. Jenike Reply

SIR: Dr. Cialdella and Professor Boissel raise several thoughtful points regarding our article. We used the term "meta-analysis" in its loosest form, that is, "combining results from different analytic studies" (1, p. xiii). We specified in our Discussion section that we did not intend to conduct a "statistical meta-analysis" or to generalize our findings beyond "four studies performed by the same investigators."

They ask why we did not combine our data with those from other studies and also suggest that we should have calculated a confidence interval around the effect sizes for each medica-

tion. At that time, there were very few open or controlled trials of these medications. Thus, we decided to report only the results of our experience with similar patient populations and using the same outcome measure for each study. As we noted, it would have been impossible to present a confidence interval with a single effect size for each medication, since the standard deviation of a single number is zero.

Our use of the pretreatment-posttreatment effect size is questioned, since it results in an overestimation of the true value of the effect size. We agree that the between-group effect size is preferable, because it takes into account nonspecific effects of treatment. However, it is often difficult to find enough placebo-controlled studies that report the necessary information for making these calculations (2). Since many studies are conducted as open trials, have crossover designs, or use comparisons with an active medication rather than placebo, the pretreatment-posttreatment effect size is often calculated from the group receiving the treatment of interest in each study, to obviate the need to discard many or most of the usable studies (1, p. 40; 2).

Since our manuscript was completed, multicenter controlled trials of clomipramine (3), sertraline (4), and fluvoxamine (personal communication, Reid-Rowell Pharmaceutical Co.) have been completed. As we have said, we found that all but one of these reports gave insufficient information for calculating between-group effect sizes. When we again calculated pretreatment-posttreatment effect sizes, as described in our article, we found effect sizes of 1.45 ± 1.68 (mean \pm SD) for two populations in the clomipramine trial, 1.02 for the fluvoxamine trial, and 0.78 for the sertraline trial, yielding effect sizes virtually identical to those we reported in our article and again giving a negative rank correlation with both serotonergic potency and selectivity of the agents. For comparison purposes, we found pretreatment-posttreatment effect sizes for the placebo groups ranging from 0.14 to 0.25 (3, 4). We hope that future studies will allow direct comparison of the efficacy of these medications in controlled trials.

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LEE BAER, PH.D.
MICHAEL A. JENIKE, M.D.
Boston, Mass.

Hypersensitivity Reexamined

SIR: A number of unwarranted conclusions were drawn by the authors of the recent case report "Exaggerated Sensitivity to an Organophosphate Pesticide" (1). The 64-year-old patient was reported to have had a long history of recurrent depressions requiring psychiatric treatment before his home was treated for termites. While the authors attributed his

physical and psychiatric symptoms for the next 2 years to this exposure to pesticide, common psychiatric diagnoses offer a more likely and parsimonious explanation. Anxiety, trouble breathing, irritability, fatigue, abdominal pain, nausea, and headaches, as reported by this patient, are all frequent complaints of depressed and anxious patients. Delusions of being poisoned are common in patients with psychoses. Irritation of mucous membranes is a difficult symptom to assess clinically and may be caused by a variety of factors. While "anticholinergic antidotes . . . offered minor relief," we were not given details of the drugs or their administration and, most importantly, we were not told whether they were given in a placebo-controlled, double-blind fashion. We were told, "He has shown evidence of sensitivity to other environmental chemicals, for example, those emanating from new furniture and carpets, as well as to a variety of psychotropic medications." Is this truly evidence, or is it attribution of symptoms? Clearly, patients such as this one are suffering, but probably not from clinical sensitivity or allergy.

Followers of the continuing controversy that envelops environmental hypersensitivity disorder (also known as total allergy syndrome, twentieth-century disease, chemically induced immune dysfunction, environmental illness, etc.) are aware that scientifically reputable task forces from the American Academy of Allergy and Immunology (2), the California Medical Association, and the American College of Physicians (3) have issued critical appraisals of the theory, testing methods, and treatments proposed by the proponents of this unproven disorder. An increasing number of reports in peer-reviewed medical journals show a high prevalence of psychiatric disorders in these patients, both currently and antedating the exposure to the "environmental toxin" (4, 5).

While there is reason to take a toxic exposure history of psychiatric as well as medical patients, there is also reason to use clinical judgment in assessing the correctness of patients' attributions of their symptoms. Clearly, more scientific information is required to assess an attribution to chemical toxicity as compared to demonic possession, but neither should be accepted without question. Psychiatrists should be aware of the documented neurotoxic effects of specific chemicals but should be extremely cautious about jumping on the bandwagon of environmental hypersensitivity.

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DONNA E. STEWART, M.D.
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Dr. Rosenthal Replies

SIR: Dr. Stewart correctly notes that it is difficult to pinpoint the exact cause of a psychiatric patient's symptoms and that the patient's attributions may not be correct. On the other hand, she notes that "there is reason to take a toxic exposure

history" and then to "use clinical judgment." Although the patient in question had a psychiatric history going back several decades, the pattern of his symptoms changed dramatically following the termite treatment of his house and took on a powerful environmental reactivity that he had not previously reported despite having had ample opportunity to do so. This feature might imply that a new causal agent was now at work in an individual previously susceptible to various influences. Such a line of reasoning would not only validate the patient's sense of reality, which appeared intact, but might also lead to useful approaches to treatment. In contrast, an unduly skeptical mind may miss important new directions in clinical psychiatry by attributing novel symptoms to "common psychiatric diagnoses."

NORMAN E. ROSENTHAL, M.D.
Bethesda, Md.

Déjà Vu Phenomena

SIR: The fascinating and provocative report on déjà vu by Herman N. Sno, M.D., and Don H. Linszen, M.D. (1) has justifiably been widely publicized. I would like to offer pertinent comments based on decades of study of déjà vu and related phenomena (2).

First, Dr. Sno and Dr. Linszen's sole cinematic example, head trauma resulting in déjà vu in Susan Seidelman's *Desperately Seeking Susan* (1985), is intriguing, but these authors, other déjà vu scholars, *Journal* readers, and people in general probably would gain a deeper understanding of déjà vu and possibly have a more remarkable cinematic experience if they were to see Ealing Studios' *Dead of Night* (1945), available on video. This is a five-part story set in rural England. The mood and mode are formed when the architect/protagonist, who has just driven to a small farmhouse, addresses a psychiatrist at a social gathering as follows: "I've seen you in my dreams—it sounds like a sentimental song, doesn't it?" The architect indicates that he does not remember how his dream ends, but he does recall that shortly after awakening he has forgotten his dream. These statements provoke others in the group to tell stories of strange occurrences in their lives. As the stories close, the viewer sees the architect awaken, implying that the preceding events were only a dream. The film ends as it began: the architect drives toward the farmhouse to experience the premonition in his dream. The power of this movie is such that, regarding the fifth segment, it was said (3) that "after Michael Redgrave played the insane ventriloquist in *Dead of Night*, bits of the character's paranoia kept turning up in his other performances."

Second, the imagery of floating audio tape recorder heads justifying holography as a mnemonic model to explain the déjà vu phenomenon is so delightfully and deliciously imaginative that I was forced to think analogously of quantized energy states (eigenstates) of charge and flux modes coupled by a tunneling frequency so that there could be a quantum superposition of states (4). These macroscopic eigenstates have been probed in an attempt to address the question of whether such a state could be captured. This is equivalent to asking whether we could see Schrödinger's notorious cat (5) in a superposition of "live" and "dead" states. Allan Widom pointed out the difficulties of measuring such states by "his claim to be able to exist quite happily in a superposition of macroscopic states—say, inside and outside the lecture theatre—so long as everyone looked the other way" (cited by Ball [4]).

I eagerly anticipate future déjà vu studies that we have not "already seen."

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STEVEN R. KOHN, M.D.
New Haven, Conn.

SIR: I was pleased to read the excellent and informative article on the déjà vu experience. The authors offered explanatory theories that had to do with psychological hypotheses involving the personal unconscious and its memories. While these are interesting and credible theories, I would like to suggest that the collective unconscious and its memory may be equally or more important in explaining déjà vu phenomena. Recently, my colleagues and I carried out a research project (1) that provides evidence supporting Jung's (2) evolutionary construct of a collective (archetypal) unconscious and its associated memory.

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DAVID H. ROSEN, M.D.
College Station, Tex.

SIR: I found the article by Dr. Sno and Dr. Linszen concerning the déjà vu experience to be extremely interesting and well-written. The historical notes, in particular, helped put the phenomenon in perspective, and the explanatory hypotheses and models were well presented. However, I believe that comments which were made regarding flashbacks and the potential clinical significance of déjà vu experiences need to be addressed.

While it is perhaps to some degree a matter of semantics, I would take exception to the contention that "the déjà vu experience must be differentiated from such phenomena as flashbacks" (p. 1588). Flashbacks vary in form and intensity depending on a number of factors, such as the type of psychedelic drug used, the duration of use, the amount of use, and the time since last use. Thus, it should not be surprising that patients often describe their flashbacks in terms of a sense of familiarity or déjà vu. In addition, there may be another possible relation between flashbacks after psychedelic drug use and the déjà vu experience, namely, similar triggers or neuropsychological mechanisms. For example, although this was not addressed in the article, it is likely that olfactory triggers (i.e., odors, pheromones) and olfactory memory are implicitly involved, at least in some cases, in causing or contributing to the phenomena of flashbacks and déjà vu.

In relation to the potential clinical significance of déjà vu, I agree with the authors that reports of the phenomenon by patients can add to the patient database. However, their use-

fulness is severely limited by the fact that, as noted by the authors, the déjà vu experience is a "ubiquitous" phenomenon and can occur even without "impaired functioning of the brain." It is probably true that the déjà vu experience, at least in the majority of cases, may simply reflect a nonpathologic cognitive experience, and as such, one can appreciate why it has not been included in *DSM-III-R* and why it is unlikely to be included in *DSM-IV*.

LOUIS PAGLIARO, PHARM.D., PH.D.
Edmonton, Alta., Canada

SIR: Dr. Sno and Dr. Linszen's hologram model of déjà vu is an intriguing idea. However, the particular example given to illustrate the model seems to ignore the large neuropsychological literature on facial recognition. This has been well reviewed by Bruce and Young (1), who suggest that a set of structural codes, with some codes describing the global configuration of the face while others represent distinct features, is used for recognition of familiar faces. Such a system is necessary, for example, for a well-known person to be recognized either on the basis of a picture of her eyes alone or a picture of her face while she is wearing sunglasses; a hologram model of facial recognition would have difficulty explaining this ability. One might therefore propose that it is common structural codes, shared by apparently dissimilar faces, that may, on occasion, trigger déjà vu.

The hologram model seems unnecessarily technological. Proust (2), the "porcelain psychologist" of his society friends, writing at the turn of the century, described déjà vu occurring when "the sensation common to past and present had sought to recreate the former scene around itself." The sensation may be a small part of both scenes, but the sensation itself, rather than corresponding sections of holograms of two rather different sensations, is identical across the two scenes. Smells may be particularly effective in evoking déjà vu. Proust again: "But when from a long-distant past nothing subsists, . . . taste and smell alone, more fragile but more enduring, . . . remain poised a long time, . . . amid the ruins of all the rest; and bear unflinchingly, in the tiny and almost impalpable drop of their essence, the vast structure of recollection."

Proust was also aware of the difference between affective and cognitive processing of percepts and memories. Marcel, Proust's narrator, "understood clearly that what the sensation of the uneven paving-stones, the stiffness of the napkin, the taste of the madeleine had awakened in me had no connection with what I frequently tried to recall of Venice, Balbec, Combray." Such a distinction seems fundamental to understanding the mechanism of déjà vu. Mandler (3) has proposed that recognition involves two separate, possibly parallel, processes: one, the detection of familiarity; the other, the retrieval of the identification of the object in terms of its previous contexts. The detection of familiarity seems to involve the arousal of an affect, viz., the sense of familiarity.

It seems not unlikely that identification of scenes similarly involves a dual process. Double orientation for place may, in some patients, be a result of conflict between the affective and the cognitive response to the environment. Fisher (4) reports a patient who describes how, on the one hand, "I've learned I should say 'Massachusetts General Hospital, Boston,'" and on the other, "but I feel I'm still at the German boundary."

I would propose that in déjà vu there is a similar mismatch between the affective and cognitive processing of information as a result of some aberrant activity in the pathway responsible for affective interpretation of percepts.

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London, England

Dr. Sno and Dr. Linszen Reply

SIR: We thank Dr. Kohn for bringing to our attention the movie *Dead of Night*. His additional explanatory theory based on "eigenstates" seems interesting but, unfortunately, probably due to our limited knowledge of the subject, not fully intelligible.

Dr. Rosen's suggestion about the collective unconscious and its memory certainly merits extensive reflection, although we are not as confident of its importance. We believe that there is no ultimate and universal explanation. In our opinion, the déjà vu experience can be produced by several of the mechanisms suggested by various theories.

We concur with Dr. Pagliaro's opinion that the déjà vu experience and flashbacks are two closely related and sometimes similar phenomena. We did not take into account the fact that users of LSD and heavy users of cannabis can experience flashbacks repeatedly and that this experience can refer to the same earlier experience(s). Thus, it is plausible that these are accompanied by a sense of familiarity. However, in that case, the criterion of the undefined past of the déjà vu experience is lacking. As to the clinical significance, nearly every psychopathological phenomenon has its counterpart in the domain of normal cognitions, emotions, and behavior. In our opinion, the psychopathological aspects of déjà vu are underestimated. For that reason we disagree with Dr. Pagliaro's prediction that the déjà vu experience will not be included in *DSM-IV*.

We thank Dr. Fleminger for his comments and for bringing to our attention the publication by Bruce and Young. We certainly agree about the importance of the neuropsychological literature on facial recognition in the context of the study of déjà vu experience. However, we did not "ignore" this part of the literature. As psychiatrists we have confined ourselves to the psychiatric literature. As stated in our article, the déjà vu experience served as an intriguing point from which to approach the study of the processes of memory storage and perception. The examination of the neuropsychological literature will be the next step.

We concur with Dr. Fleminger's opinion that the merit of holography as a mnemonic model is limited. The theory of Bruce and Young seems interesting and plausible. Instead of a substitution, we tend to regard this theory as an additional hypothesis. The famous déjà vu experience of Proust, induced by the *petites madeleines*, can also be regarded as an example of reintegration, in which an impression of familiarity with the whole present situation is elicited when a part of an unconscious memory recurs in the present (1). In a future paper we shall detail the defensive aspects of this and another déjà vu experience described by Proust that has been previously analyzed by Pickford (2).

We wholeheartedly agree with Dr. Fleminger that the déjà vu experience can be the result of a conflict between affective

and cognitive processing of information. Accordingly, as stated in our article, we regard the experience as a disturbance of apperception (i.e., perception modified by one's emotions and thoughts). Our opinion about the influence of affective factors also manifests itself in the extensive discussion of the psychodynamic explanations.

However, this influence is not a *conditio sine qua non*. The mismatch can also be a result of either a disturbance in cognitive processing itself (e.g., a memory disorder, an attention and thinking disturbance) or an organic lesion (e.g., temporal focal epilepsy, cerebrovascular accident). We believe that there is no ultimate and universal explanation and that, as we have said, the déjà vu experience can be produced by several of the mechanisms suggested by various theories.

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HERMAN N. SNO, M.D.
DON H. LINSZEN, M.D.
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Object Relations in Adolescent Girls

SIR: The excellent article by Drew Westen, Ph.D., and associates on the impact of developmental history on object relations in adolescent girls (1) suffers from one problem in the interpretation of the data. The authors attempt to test the theory that early childhood (which they call "preoedipal years") is crucial for object relations. Their index of risk factors includes premature delivery, maternal borderline personality disorder, "difficult" infancy, separations and losses, and abuse. Recognizing that not all of these factors are phase-specific, the authors removed the first two, and the relationship remained significant. However, it is not clear that the remaining variables are phase-specific either. Temperamental qualities such as being "difficult" in infancy have been shown to continue throughout childhood (2). If temperament is being picked up by these reports, this variable may relate to increasing evidence of biological factors in impulsive personality disorders (which were frequently diagnosed in this sample). Separation and losses in early childhood have been shown to predict later psychopathology only when interacting with many other later events to produce a cascade of risk factors (3). Abuse in early childhood would also reflect pathological family settings with long-range effects. The failure of the latency risk factors to predict object relations could easily reflect less severe family pathology and less severe constitutional vulnerability when difficulties are apparent only later in childhood.

I am sure the authors recognize the difficulty of interpreting such complex relationships. They acknowledge, as well, that sexual abuse which occurs later in childhood has a powerful effect on how the object world is perceived. But in their trying to fit their data into the Procrustean bed of psychoanalytic developmental theory, one feels a sense of strain. There is scant support in the literature for the idea of critical periods in early childhood (4). The best models appear to reflect the cumulative effects of multiple experiences over longer periods of time (5).

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JOEL PARIS, M.D.
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Dr. Westen and Dr. Ludolph Reply

SIR: We are largely in agreement with Dr. Paris's suggestion that the etiology of pathological object relations involves an interaction of many different factors, biological and environmental, and that psychoanalytic theories have oversimplified issues by suggesting that all severe character pathology has its roots in the preoedipal period. Poor caregiving and disruptions in the attachment relationship in the first few years by parents whose object relations are themselves pathological are probably good predictors of poor caregiving, family chaos, and disrupted attachments later in childhood. Thus, isolating a single variable in a single period is extremely difficult methodologically and highly problematic theoretically. One of us has, in fact, recently written extensively about the problematic assumptions, etiological and otherwise, of object relations theories (1, 2). On the other hand, pathology in a family system—such as multiple parental surrogates coming in and out of the family unit or children being sent many times to live with different caretakers—cannot be divorced from the object relations disturbances of the people who create that system. Many of the risk factors isolated by researchers interested in the etiology of disorders such as depression may thus themselves be in part epiphenomenal.

With respect to Dr. Paris's concern that we might have been trying to force the data into a Procrustean bed (or preoedipal crib), in fact, we only created the composite age-specific risk variables as a data reduction strategy to try to guard against the possibility that our more specific findings would occur by chance. We were, ourselves, extremely surprised by the outcome. As to specific variables included in the preoedipal risk factor index, abuse, neglect, separations, and so forth were coded for the age at which they occurred, and the composite index including similar variables after age 5 was not similarly predictive of object relations pathology. The size of the correlations between the preoedipal risk variable and the object relations variables might be altered somewhat by deleting particular variables, but the correlations were by and large so strong that this would not be likely to have much of an impact on interpretation of the findings.

Overall, we suspect, with Dr. Paris, that object relations pathology cannot be reduced to a single cause for all patients. Nevertheless, one does not need to extrapolate far from the ethological data and from contemporary attachment research (3) to suggest that expectations of relationships and behavioral patterns that influence subsequent relationships begin to take clear form in the first 4 years of life; consequently, early childhood is likely to be a particularly important, but probably not decisive, period for the development of object relations.

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DREW WESTEN, PH.D.
PAMELA LUDOLPH, PH.D.
Ann Arbor, Mich.

Increased Risk of Stroke in Patients With Panic Attacks: Real or Perceived?

SIR: Myrna M. Weissman, Ph.D., and associates (1) reported that subjects with panic disorder and other psychiatric disorders were at higher risk of having hardening of the arteries, high blood pressure, heart attack, and stroke than subjects with no psychiatric disorder. Subjects with panic disorder had a risk of stroke twice as high as that of persons with other psychiatric disorders or no psychiatric disorder. These conclusions were based on respondents being asked simply "if they ever had hardening of the arteries, high blood pressure, a heart attack, or a stroke." Although Dr. Weissman and associates admitted that medical examinations and laboratory tests were not conducted, they referred to these "diagnoses" only once as "self-reported" problems (in table 2). Throughout the article the authors used language that implies that these were medical diagnoses and real clinical risks. However, these statistical associations are as likely to be related to a subject's anxiety over physical sensations as to real medical pathology. The researchers acknowledged this methodological weakness in a separate article (2), emphasizing that persons with panic attacks have "substantial impairment in perceived physical and emotional health" and "often believe that they are seriously physically ill and seek medical attention." It is unclear why, in this separate article published in another journal, the authors were careful to refer to subjects' "perceived" medical problems, while in the article in the *American Journal of Psychiatry*, these perceptions became risks for real medical illness.

Dr. Weissman and colleagues miscited Martin et al. (3), stating that these investigators found "a significant association between cardiovascular or cerebrovascular mortality and panic disorder." Martin et al. actually found that "mortality was not excessive among patients with primary anxiety neurosis or hysteria" (3, p. 53). Because of the diagnostic criteria used by Martin et al., most of their anxiety neurosis group appear to have had some form of panic attacks. Examining the cause of death in part II of their article (4), Martin et al. reported only three deaths among the patients with anxiety neurosis; one died of a malignancy and two committed suicide. Hence, these data do not support Dr. Weissman and associates' conclusions, since mortality was *not* excessive for patients with anxiety neurosis and *no* deaths resulted from cardiovascular or cerebrovascular disease.

Finally, it seems premature for the authors to speculate about "possible mechanisms to explain the association" between panic disorder and stroke, since their data lack scientific validation that the "strokes" existed beyond the minds of their panic disorder subjects. I hope that future studies will apply medical diagnostic criteria more stringently so that readers of the *Journal* can be confident that the risks of medical complications are real and not imagined.

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EARL A. BURCH, JR., M.D.
New Orleans, La.

Dr. Weissman and Associates Reply

SIR: We appreciate Dr. Burch's close attention to our article reporting data from the Epidemiologic Catchment Area (ECA) study. We felt that the association between panic disorder and cardiovascular/cerebrovascular problems found in that study should be reported, so that investigators would be alerted to the possibility that the association might not just be a misperception and deserves further study.

We believe that our epidemiologic findings are consistent with the Haines et al. follow-up study (1) of men, ages 40-64, which found that an initial high score on phobic anxiety was strongly related to subsequent major ischemic heart disease 6 years later, as well as the finding of Coryell et al. (2, 3), in a 35-year follow-up of inpatients with panic disorder, of an increased mortality rate in men due to cardiovascular or cerebrovascular disease. Additionally, the findings of Kahn et al. (4) that panic disorder is associated with cardiomyopathy and also with enlargement of the left ventricle were consistent with increased risk for cardiovascular accident.

While we have previously reported from the ECA study that persons with panic disorder feel that they are in poor physical health, they did not differ in this regard from persons with major depression in the same ECA sample (5). However, major depression in the ECA study was not associated with the similar reports of cardiovascular/cerebrovascular problems.

We agree with Dr. Burch that our use of self-reported medical diagnoses is a caveat worth emphasizing, and we believe our article did so. We disagree with Dr. Burch that we referred only once, in table 2, to the medical illnesses as self-reported problems. The abstract (p. 1504) and the Discussion section (p. 1506) clearly stated that medical examinations were not done.

Dr. Burch is, however, correct that Martin et al. did not find an excess mortality in subjects with anxiety neurosis, possibly because about 50% of their sample was under age 35 initially and thus, at most, only 7 years older at follow-up. The Martin et al. reference was incorrectly included along with the others, which are correct as stated.

We agree with Dr. Burch that future clinical studies following up these associations noted by Coryell et al., by Haines et al., and, now, in the ECA study require careful medical and psychiatric examinations as well as laboratory tests. These studies may clarify what is real and what is misperceived, and whether there are important subgroups of patients with panic symptoms and panic disorder.

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Opiate System in Self-Injurious Behavior

SIR: Ronald M. Winchel, M.D., and Michael Stanley, Ph.D., in their article on self-injurious behavior (1), reviewed various aspects of this often intractable and devastating syndrome, including the possible role of the opiate system. While clinical use of opiate receptor antagonists was reviewed, no mention was made of the use of agonists.

Many characterological self-mutilators have histories of childhood abuse. It is clear that pain (perhaps psychological as well as physical) leads to increased brain levels of endorphins. A possible psychophysiological mechanism would be habituation to high endorphin levels in childhood secondary to repeated physical abuse. At times of stress, the (now adult) patient raises endorphin levels by self-inflicted pain.

I wonder whether our colleagues in methadone maintenance programs have observed any change in self-mutilating behavior in individuals in whom self-mutilation and opiate addiction have coexisted. Given the severity and often life-threatening nature of this syndrome, a study of methadone maintenance on a double-blind basis would seem warranted if supported by naturalistic observation.

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STEPHEN J. CHERNAIK, M.D.
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Dr. Winchel and Dr. Stanley Reply

SIR: Dr. Chernaik raises the interesting possibility that naturalistic observations of opiate abusers, or methadone-treated individuals, may shed light on theories of the involvement of opiate dysregulation in self-injuring behavior. This possibility occurred to us, and in preparing our review we searched the scientific literature and spoke with colleagues experienced in the treatment of opiate dependency.

The only association between drug abuse and self-injury that we found was the well-known observation that many pa-

tients with cocaine dependency experience unusual skin sensations, which may occasionally lead to significant self-excoriation. While this behavior may appear similar to "neurotic excoriation," which has been reported to respond to treatment with an opiate antagonist (1), it offers little value in understanding potential opiate mechanisms in self-injuring behavior. (Cocaine's principal actions are mediated through the dopaminergic system, which does interact with opiate systems, but this is an insufficient basis for postulating opiate mediation of self-injury.) We found no observations that associated methadone treatment with self-injury.

The idea is a good one, nevertheless. However, because of the potential problems (such as dependency formation) in administering opiate agonists to patients, such treatment studies should first be justified by strongly validated observations of opiate effects on self-injury. Studying the behavior of opiate-dependent individuals is severely complicated by the neuropsychiatric effects of drug abuse. The use of methadone in the treatment of these individuals may provide an opportunity to add prospective evaluation of self-injury histories as patients are beginning methadone treatment. Prospective studies of these patients (including self-injury history prior to the onset of substance use, as well as evaluations of self-injuring behavior at the time of methadone discontinuation) may add support to concepts of opiate dysregulation in self-injury. Because of the high incidence of both substance abuse and self-injury in prison populations, these might provide useful settings for such studies.

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Trauma and Dissociation

SIR: In the continuing investigation of the role of trauma in the development of dissociation and related states, many authors have tried to demonstrate a direct link between a history of childhood trauma, usually some form of abuse, and the subsequent development of dissociative defenses or pathology. The article by Barbara Sanders, Ph.D., and Marina H. Giolas, M.A., entitled "Dissociation and Childhood Trauma in Psychologically Disturbed Adolescents" (1) represents a relatively sophisticated empirical attempt to address this question. However, in discussing their findings, the authors appear to have strained to fit the findings into a "trauma causes dissociation" framework, to the neglect of their obtained results.

The authors stated that the purpose of the study was to "test the hypothesis that dissociation in adolescence is positively correlated with stress or abuse experienced earlier" (p. 50). In so doing, they failed to define, at the outset or at any point in the article, their use of the term "childhood stress." In my opinion, this fundamental failure sets the stage for a more serious lapse resulting in a misrepresentation of their reported findings.

The authors reported that the correlations they obtained between scores on the Dissociative Experiences Scale and the various scales of the child abuse and trauma questionnaire ranged from 0.26 for sexual abuse to 0.50 for negative home environment. However, in their discussion of these findings,

most of their emphasis was placed on the pathogenetic nature of the trauma experience. The basis for this finding appears to derive from the correlation between the overall questionnaire score and the Dissociative Experiences Scale score. The failure of the authors to address adequately the unique variance of the scales and the probable intercorrelations among the questionnaire scales in their population make their claims about the primacy of abuse experiences in the development of dissociation highly questionable. Indeed, taking only their reported correlational findings, the focus of the discussion could have readily been assumed to be on the role that a negative home environment plays in the development of dissociative phenomena.

The methodological shortcomings in this article are noteworthy not only in themselves but inasmuch as they illustrate a trend in the abuse-dissociation literature to pursue this link often without regard to potentially confounding variables that have long been known to be related to adult functioning, i.e., the nature of the early childhood family environment. This issue is nicely addressed in another article in the same issue of the *Journal*, the investigation by Philip G. Madonna, M.S.W., and associates (2) of the relation between family interactional style and incest. In fact, an emerging literature on the relation between trauma, family functioning, and subsequent psychopathology is emerging (3). Steps toward an integration of the impact of the environment into which trauma emerges and by which trauma is often sustained with the specific role of trauma in producing dissociation and other maladaptive responses would seem a necessary and prudent step in the evolution of a comprehensive theory of the relation between childhood experiences and subsequent functioning.

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TIMOTHY L. HULSEY, M.A.
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Dr. Sanders Replies

SIR: Mr. Hulseley points out, quite correctly, that our study made no attempt to isolate any possibly unique variance associated with any specific subscale of the child abuse and trauma questionnaire. In other words, we have not tried to distinguish between effects produced by, for example, sexual abuse and those produced by, say, neglect. There are several reasons for this, one very important one being that the subscales defined in our article are based on a conceptual sorting of the items rather than a factor analysis. We described them separately to illustrate the content domains that are tapped by our instrument; however, we cannot assume that these clusters do, in fact, constitute distinguishable dimensions of childhood experience. Our sample size in this study was a bit small for a factor analysis.

We have recently completed a factor analytic study of a slightly revised version of this questionnaire with a large sample of college students. The subscales identified in that study were similar to, but not identical to, the scales defined in our

article. Importantly (and not surprisingly) they are not orthogonal. Future research with these empirically determined subscales might more appropriately address the issue of whether dissociation is more highly correlated with some types of childhood experiences than with others. Even so, differences in the magnitude of the correlations of the several child abuse and trauma scales with the Dissociative Experiences Scale might be produced by differences in the adequacy of assessing the various aspects of childhood experience rather than by differences in the relevance of the different experiences for later dissociative capabilities. In short, the question Mr. Hulsey raises is not as easy to answer as it might at first appear, and it is not appropriately addressed with the present data.

While acknowledging that we have not attempted in this research to distinguish among various environmental causes of stress, we do not accept the charge that we, to use Mr. Hulsey's words, "have strained to fit the findings into a 'trauma causes dissociation' framework." In our initial study of dissociation in college students, we showed that responses to the question "How stressful was your childhood?" correlated significantly with dissociation. The present study replicated this correlation and also documented that a variety of childhood experiences, all of which may reasonably be assumed to be stressful or even traumatic, correlate with the stress question and also correlate with degree of dissociation. Our conclusion is that the greater the childhood stress, from any or all of several sources, the greater the frequency of dissociative experiences. Other research must address the question of whether particular types of events are more likely to produce dissociation than other types. My own hunch about this is that in the domain of the young child's experiences at the hands of family members or principal caretakers, the victim's *perception* of trauma will prove to be more important than the particular means by which the trauma is inflicted.

BARBARA SANDERS, PH.D.
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Credibility of Patients in Psychiatric Research

SIR: Each month, after I read the *Journal* from cover to cover, I sit and ask myself, What does it all mean, and what do we know for certain? Some months, it seems as though +2 added to -2 comes to 0. Take the January 1991 issue, for example.

Kathleen M. O'Leary, M.S.W., and associates (1) begin their article with the comment—a fair one, I think—that "the clinical literature on borderline personality disorder is replete with examples of memory impairment and cognitive distortions . . . in daily life . . . hysterical style characteristic of patients with borderline disorders . . . histrionic features . . . 'tendency toward global perceptions with a loss of attention to details, distortion of the meaning of an event, patterns of confusion and spotty amnesias.'" The article, among other conclusions, confirms quite reasonably that the factual credibility of the borderline-histrionic-dissociative cluster of individuals might be considered less than perfect. I did not find that surprising, but thought this an interesting article. Whether these individuals' lack of factuality and/or truthfulness is conscious or unconscious is another matter.

However, the same issue of the *Journal* contained two articles that relied in their absolutely essential features upon accepting the credibility of just such individuals. George R. Brown, M.D., and Bradley Anderson, M.D. (2) found "dramatic confirmation of the high prevalence of borderline per-

sonality disorder in adults who report childhood histories of abuse" by asking adult patients questions about their childhood. When patients are asked about abuse and how others treated them, many more borderline patients than others will confirm that they were treated badly, although at times "repeated questioning is necessary" to produce this result.

Similarly, Barbara Sanders, Ph.D., and Marina H. Golas, M.A. (3), surveying the responses of adolescents prone to dissociation (not a group that most lawyers would term "credible witnesses") wrote, "The principal finding . . . is that the child abuse and trauma questionnaire . . . correlated significantly with the frequency and extent of dissociative experiences." One could undoubtedly question these adolescents about a good many things and produce interesting correlations and comparisons to others whose mind set is more objective.

If it is true that the memories and perceptions, and perhaps the truthfulness, of individuals in the borderline-histrionic-dissociative cluster are less reliable and credible than ordinary average human memory, which is none too good, what does the administration of questions to such individuals prove about causation? After all, I can quote no less an authority than the *American Journal of Psychiatry* to the effect that "the clinical literature on borderline personality disorder is replete with examples of memory impairment and cognitive distortions." These persons appear to have poor memories, they distort, they ignore details and little things like facts in favor of global impressions and proving that things are whatever they feel them to be, and they are prone to blame others. We must not permit ourselves to think that they lie, as that would be wholly inadmissible to modern, enlightened psychiatrists. But they can "dramatically confirm" almost anything they want or someone else induces them to want.

It is a bit wearisome to reflect that if a psychiatrist who had been dead for 100 years were to come to life to join this discussion, he could leap right in, needing only a few new buzzwords. So where were we in January 1991, and what do we know for certain?

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Drs. Brown and Anderson and Dr. Sanders Reply

SIR: Dr. Furlong seeks to indict the last 100 years of psychiatry as coming "to 0," using three articles (including ours) in the January 1991 issue of the *Journal* as cases in point. He begins his comments by incorrectly attributing the quotation from Kroll (1) regarding the cognitive deficits of some patients with borderline personality disorder to Ms. O'Leary and associates. He then proceeds to paraphrase his understanding of the main conclusions of their work to include (in his words) the "lack of factuality and/or truthfulness" in patients with borderline personality disorder. Kroll spoke of a loss of *attention* to details and distortions of *meanings* of events, not to

outright fabrication and "lack of factuality" in the reporting of events, as Dr. Furlong suggests. After a careful reading of the article by Ms. O'Leary and colleagues, we fail to find that these authors concluded that patients with borderline personality disorder concoct answers to questions asked of them; rather, their unreliability as historians was largely limited to missing data, much of which was readily retrievable with cues. In fact, the performance of patients with borderline personality disorder on complex memory tasks was nearly identical to that of control subjects after cues were provided. Although the authors did not test for long-term memory dysfunction, if this deficit were also present, we could speculate that an even greater number of the patients with borderline personality disorder in our own study had past histories of abusive experiences which they were unable to retrieve and that more such experiences may be lurking in the past of those who could recall some of them during our interviews. Interestingly, our technique of repeated questioning could be interpreted as an auditory cue consistent with one of the suggestions made by Ms. O'Leary and associates for assisting these patients to retrieve forgotten material.

Dr. Furlong seems to suggest that our conclusion is that childhood abuse histories "prove causation" of borderline personality disorder. It is certainly possible that such events can play an etiological role in the development of the disorder (2), along with many other complex psychosocial factors and neuropsychiatric factors that may have genetic origins (3). It would be both premature and unwise to suggest that our observations in any way prove causation. We note, however, that the work of Ms. O'Leary and associates is supportive of our findings of extensive adult psychopathology in patients likely to have developed the antecedents of borderline personality disorder in childhood. Learning from adverse life events may be impaired in these children, leading to repeated poor choices in relationships and other life decisions that perpetuate psychic trauma and maladaptation. To remain within the boundaries of their data, Ms. O'Leary and colleagues also cautioned us against extrapolating from their unreplicated data on 16 carefully selected "research outpatients with borderline personality disorder" to all patients with this disorder.

Last, we are disturbed by Dr. Furlong's implicit accusation that our research interviews with patients sought to confirm previous findings on borderline personality disorder by "inducing them to want" to report such histories. Such research practices would be, at the least, careless and, at most, highly unethical. One of our interviewers was blind to the hypotheses of our study. Furthermore, Dr. Furlong's criticism is rendered moot by the fact that all three papers we quoted whose results were supported by our work were published well after our study was underway.

Dr. Furlong concludes his comments by asking, "What do we know for certain?" We should *know*, as psychiatrists, that the difference between forgetfulness and fabrication is vast. We should *strongly suspect*, on the basis of an ever-increasing body of careful scientific work, that childhood experiences that include repeated physical and/or sexual abuse can play a major role in adult psychopathology. Those are not just "buzzwords."

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SIR: For any verbal report measure, what we know depends on how willing we are to believe our subjects. Dr. Furlong singles out borderline patients as particularly unreliable and, by casual extension, questions the credibility of what he terms the "borderline-histrionic-dissociative cluster." This cluster includes the dimension we attempted to isolate in our own work, i.e., dissociation, although the relevance of the cited empirical findings on borderline subjects is of dubious relevance to our patients. What we showed is that dissociation is correlated with self-reported childhood trauma in patients across different diagnostic categories. Importantly, we noted that patients high in dissociation were distributed across various diagnostic categories, including but not limited to the following: mood disorder, attention deficit disorder, eating disorder, conduct disorder, personality disorder, adjustment disorder, and substance abuse disorder. In a previous study (1) my colleagues and I found that normal college students who reported more frequent dissociative experiences also reported more stressful childhoods.

The correlation between dissociation and childhood stress in the mixed psychiatric sample and in normal subjects cannot be attributed simply to unreliability of reporting, even if one chose to view dissociation as a marker for unreliability, since mere unreliability would act to obliterate a true relationship rather than artificially to create one. One could, of course, entertain the hypothesis that individuals prone to dissociation introduce systematic bias when recalling and/or reporting their childhoods. However, the expected bias would be a tendency to minimize rather than to exaggerate trauma, which would work against the observed relationship. Evidence for this sort of bias was obtained in a study recently completed in our laboratory in which Golas (unpublished data) showed that high-dissociating college students exhibited a greater tolerance for physical pain than did low dissociators.

The hypothesis we are pursuing is that dissociation is at least in part a result of traumatic or stressful experiences. Admittedly, this hypothesis is grounded in data which, for the most part, have been obtained through self-report, and we along with many other investigators will continue to welcome and to seek data corroborating these reports. Nonetheless, the hypothesis seems more parsimonious and more fruitful to pursue than the line of discrediting the witness. As for what we have learned from history, Freud's retreat from his original "seduction theory" of hysteria is a path we are now more reluctant to tread.

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BARBARA SANDERS, PH.D.
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Water Intoxication Precipitated by Thiazide Diuretics in Polydipsic Psychiatric Patients

SIR: René J. Muller, Ph.D., and Helen D. Lann, M.D. (1) added an instructive case to the literature, highlighting the risk

of water intoxication when thiazide diuretics are prescribed for psychiatric patients who already have a polydipsic syndrome. Strongly supporting their warning, we present a similar case, and expand their warning to include other potential exacerbating agents and the risk of overzealous correction of hyponatremia.

Ms. A, a 35-year-old schizophrenic patient, hospitalized at a state facility for the preceding 7 years, was maintained on a daily regimen of fluphenazine, 30 mg; diphenhydramine, 50 mg; clonazepam, 4 mg; and levothyroxine, 0.15 mg. When it was noted that she drank excessive amounts of fluids in response to command hallucinations ("You may as well have a glass of water; go ahead, have a glass of water"), her intake of fluids was restricted to 1500 cc/day and her serum sodium levels averaged 132 mmol/liter. Hypertension not responsive to a low-salt diet and captopril led to the addition of hydrochlorothiazide, 25 mg/day, with triamterene, 50 mg/day. Six weeks later she experienced projectile vomiting and a first seizure, at which time her serum sodium level was found to be 117 mmol/liter. Diuretics were discontinued, and for the past 15 months she has been seizure free and her serum sodium levels have averaged 133 mmol/liter.

Like the patient of Dr. Muller and Dr. Lann, Ms. A had a mild, manageable polydipsic syndrome until a thiazide diuretic was prescribed, and there have been no complications since that drug was discontinued. Since many nondiuretic antihypertensive agents are available (e.g., β blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors), this is an avoidable interaction, requiring only that the physician recognize the polydipsic syndrome, which is more common than usually appreciated.

Importantly, other medications may also cause this problem. Carbamazepine not infrequently causes hyponatremia and may precipitate water intoxication in polydipsic patients. Most strikingly, Emsley et al. (2) reported that of 15 hyponatremic, schizophrenic or mentally retarded, long-term psychiatric inpatients, 13 were receiving either hydrochlorothiazide (five patients) or carbamazepine (eight patients). The hypoglycemic sulfonylureas chlorpropamide and tolbutamide can cause hyponatremia; we feel that a reported case of fatal water intoxication in a polydipsic patient (3) may have represented exacerbation by the latter agent. Fluoxetine has also induced hyponatremia (4), as have tricyclic antidepressants and phenothiazines (rarely), vincristine, and cyclophosphamide.

We wish to add another caveat: the risk of too rapidly correcting a hyponatremic state. The patient that Dr. Muller and Dr. Lann reported was rather aggressively treated (27 mmol/liter of serum sodium in 8 hours). Many clinicians, fearing the complication of central pontine myelinolysis, advise correction no faster than 12 mmol/liter per day (5).

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Managed Psychiatric Care

SIR: In his editorial "Utilization Management: Managed or Mangled Psychiatric Care?" (1), Steven S. Sharfstein, M.D., referred to the study of utilization management done by the Institute of Medicine (2). He correctly paraphrased the Institute's finding that there is little "systematic evidence" about utilization management's effect on quality and that utilization management is a "working hypothesis." He then stated that "it is a working hypothesis that places patients and providers at extraordinary economic and clinical risk." In our opinion, patients are at far greater risk outside of utilization management programs. Utilization management does place some providers, particularly psychiatric hospitals, at economic risk—as well it should.

We agree that there is little systematic evidence about the effects of managed mental health care on quality and costs. Such evidence will increase as the field matures. But the lack of such systematic evidence has not been an obstacle to the growth of psychiatric practice. Were we to wait for systematic evidence to prove the value of much that is done at Dr. Sharfstein's hospital and others, their work would be sharply reduced.

We agree with Dr. Sharfstein's statement that psychiatrists "must develop and implement cost-effective alternatives in the face of increasingly limited benefits." But the advice comes a bit late. The failure of psychiatrists and others to do so is a direct cause of the limited benefits. Fueled by excessive utilization of inpatient treatment, the outrageous cost increases of the past few years have been the major reason for the decline in benefits and growth of managed mental health care. It is ironic that those who are most unhappy about managed mental health care have done the most to bring it about.

We do not understand the basis for Dr. Sharfstein's statement that "patients have not given informed consent." The fact that utilization management is part of an employee's health benefits is clearly stated in benefit plan descriptions and other materials furnished to all employees. Further, our organization provides orientation sessions in the workplace to help employees better understand what managed mental health care is and how it works. We believe others do the same.

Dr. Sharfstein's advocacy of regulation as a "pressing social policy concern" is clearly not shared by the Institute of Medicine. In fact, the Institute report states that regulatory activities would be premature, would aggravate the inflation of health care costs, and are not justified in the absence of evidence as to the detrimental effects of utilization management.

Utilization management is, as Dr. Sharfstein suggests, "a fact of life" and will be increasingly so. All of us must work together to be certain that it enhances the value of mental health services. We hope that psychiatry will contribute to the process.

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Dr. Sharfstein Replies

SIR: Dr. Feldman and associates raise some interesting points of dispute with my editorial. Much of managed "care" is truly managed "cost," and in that context I believe that patients and providers are placed at economic and clinical risk. The evidence for this is contained in the many anecdotal reports that have been received during the past year by APA's hotline on managed care. Several hundred documented cases have come to the attention of APA that clearly indicate compromises in patient care in order to conserve third-party resources. To assume that this cost saving improves access or quality of care is extremely naive. It does improve the bottom lines of corporations and helps the growing industry of fourth- and fifth-party reviewers in the extremely effective pursuit of "rationing by harassment."

I would argue further that there is much more systematic evidence about the benefits of psychiatric treatment than the benefits of managed mental health care. I do not believe that patients are aware how much they are signing away of their confidential doctor/patient relationship when they contract for their insurance. They are often not even aware of the restricted mental health benefits they have in the first place. I agree with the authors that employees need orientation sessions about managed mental health care so that they can make informed choices when the open enrollment season for insurance benefits comes around.

Just as private health insurance is regulated by government, it is essential that private utilization management companies be regulated as well. Many states are considering such regulatory approaches, because there has been a demand for some scrutiny of the varied and capricious practices of the numerous utilization management groups.

Managed care and utilization management are often marketed in the context of a broad assault on the value of traditional mental health services. I agree with the authors of this letter that it is important to begin to discuss together the meaning of the term "value" in the delivery of mental health services and to assess the positive as well as the adverse impacts of managed care on access and quality. If, as a result of this dialogue, more patients can be treated in a broader array of outpatient and residential settings, there will be more congruence than conflict between providers and managed "care" organizations. If, instead, care is denied and payers become the principal beneficiaries of management of third-party payments, then our patients and the public will be the principal losers.

STEVEN S. SHARFSTEIN, M.D.
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Development of DSM-IV

SIR: While Allen Frances, M.D., and associates are to be commended for their substantive review of work now underway on DSM-IV (1), it appears obvious that the DSM-IV task force is repeating the developmental errors of its predecessors. Certainly, the authors' initial comments offer hope that DSM-

IV will be a great improvement. The "major innovation" will be the "emphasis on explicit documentation and review of evidence," and the "threshold for making revisions . . . [will be] much higher." Further, "decisions must be substantiated by explicit statements of rationale and by the systematic review of relevant empirical data."

Unfortunately, these highly desirable goals are in danger of being compromised by a host of other issues. These include the "crucial" need to incorporate the suggestions of hundreds of work group advisors and over 65 organizations; the need for an "optimal balance" with regard to literature reviews, tradition, ICD-10, and "common sense"; and applicability to the "widest diversity of settings," ranging from clinical work and research to disability determinations and insurance reimbursement.

I submit that the task force has set itself two mutually contradictory goals. One is the formulation of a data-based nomenclature; the other is a consensus-based system acceptable to a hodgepodge of committees and organizations, attorneys, and insurance companies.

If history is any guide, the consensus-based system will prevail. Dr. Frances and associates (2) have stated that DSM-III and DSM-III-R "were, by necessity, the result of expert group consensus." Almost 20 years ago Rosenhan (3) excoriated psychiatry for making diagnoses by consensus, but despite Spitzer's valiant defense (4), the tradition continued, as the introductions to DSM-III and DSM-III-R have acknowledged. More recently, Coryell and Zimmerman (5), noted that "changes in criteria are likely to reflect new committee membership rather than new, empirically-based knowledge."

Dr. Frances and associates claim that the imminent publication of ICD-10 was the major factor in the rapid formation of the DSM-IV task force, but surely the new ICD was no surprise, as the groups responsible for both systems have worked together for years. Whatever our treaty obligations with the World Health Organization (1), one wonders if better compatibility with ICD-10 is worth the disruption of research, revision of structured interviews, and other difficulties attendant on DSM-IV.

If our claims to neuroscientific status are to be credible, then we need a scientifically based nomenclature. Clinical studies that utilize positron emission tomography and other superb technologies have their importance diminished if the diagnostic system is compromised. Psychiatry needs to decide whether acceptability or science is more important.

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CHARLES E. DEAN, M.D.
Minneapolis, Minn.

Dr. Frances and Associates Reply

SIR: Dr. Dean's letter helps us to clarify an important point that may have led to misunderstanding. We believe that Dr. Dean has ignored the vast difference in the availability and use of empirical data in the preparation of DSM-IV as compared

to *DSM-III* and *DSM-III-R*. For *DSM-IV*, decisions are based on extensive literature reviews, data reanalyses, and carefully conducted, focused field trials—none of which were previously possible. Of course, the data generated in each of these steps must be interpreted and applied to the diagnostic questions facing the *DSM-IV* work groups.

We are subjecting our data and reviews to the scrutiny of many advisors in order to ensure that the conclusions drawn reflect a consensus understanding of the field and are generalizable to the widest diversity of settings. The use of a large cohort of advisors is to ensure the best and most representative interpretations of the data we are reviewing and generating. This procedure is meant precisely to guard against the kind of arbitrary changes Dr. Dean cautions

against. We therefore disagree with his submission that *DSM-IV* is following “two mutually contradictory goals”: a “data-based nomenclature” and “a consensus-based system.” Instead, we are attempting to establish consensus about just how best to interpret the data. We know of no better way to develop the “scientifically based nomenclature” desired by us and also by Dr. Dean.

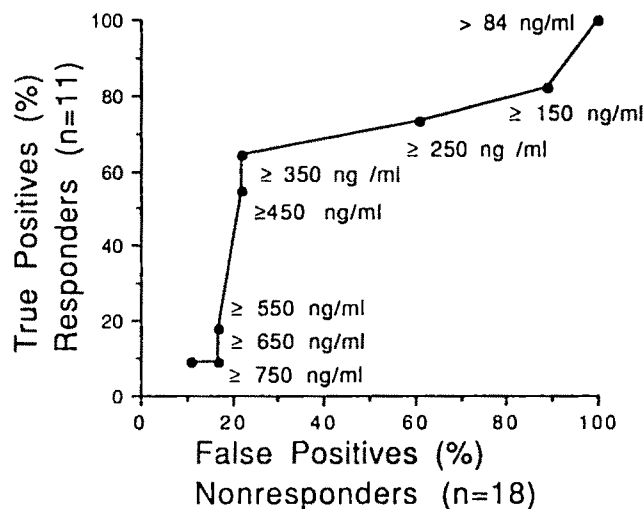
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Reprints of letters to the Editor are not available.

Corrections

The correct figure 1 for the article “Clozapine and Norclozapine Plasma Concentrations and Clinical Response of Treatment-Refractory Schizophrenic Patients” by Paul J. Perry, Ph.D., et al. (February 1991 issue, pp. 231–235) is given below.

FIGURE 1. Receiver Operating Curve for the Relation Between BPRS Scores and Clozapine Plasma Concentrations of 29 Schizophrenic Patients Treated for 4 Weeks



In the article “New York Under the *Rivers* Decision: An Epidemiologic Study of Drug Treatment Refusal” by Julie Magno Zito, Ph.D., et al. (July 1991 issue, pp. 904–909), references 15 and 16 in the reference list on p. 909 should be reversed. Reference citation 15 in the text refers to the study by Volavka et al. and reference citation 16 refers to the Zito et al. paper.

In the reply of James A. Chu, M.D., to a letter to the Editor, “Dissociative Disorders and Complex Partial Seizures,” by Wayne H. Peterson, Ph.D. (August 1991 issue, pp. 1106–1107), the attribution for the quotation beginning “Only three of seven patients . . .” is incorrect. The correct reference is as follows: Shearer SL, Peters CP, Quaytman MS, Ogden RL: Frequency and correlates of childhood sexual and physical abuse histories in adult female borderline inpatients. *Am J Psychiatry* 1990; 147:214–216.

Annual Reports to the Membership

The following are edited versions of the annual reports by the APA Secretary, Treasurer, Medical Director, Speaker, and Speaker-Elect and the chairpersons of the APA Committee on Constitution and Bylaws, Committee on Membership, and Committee of Tellers. The reports were presented at the APA annual business meeting in New Orleans on May 13, 1991.

Report of the Secretary: Summary of Actions of the Board of Trustees, May 1990–May 1991

Philip M. Margolis, M.D.

OVERVIEW

It is my personal and constitutional privilege as Secretary to report to the membership the actions taken by the Board of Trustees and some of the significant activities of the Association over the past year. The actions reported do not include a number of issues referred to appropriate components for further study and recommendation. As required by our Constitution, especially important issues will be discussed and clarified at the annual business meeting and a full report will be published in the *American Journal of Psychiatry*.

The work of the Association has proceeded at a rapid pace over the past year. Major concerns have been managed care systems, insurance coverage of psychiatric care, nonphysician prescribing privileges, prescribing and dispensing regulations related to clozapine, Medicare and Medicaid (including extraordinary investigations of allegations of fraud against physicians), practice guidelines, and membership, ethics, judicial, legal, and fiscal issues. The Association responded to the rapidly changing situation in the Persian Gulf at both the national and local levels. Initially, programs were established around the country to assist families of hostages. Mobilization of troops for Operation Desert Shield and Operation Desert Storm dramatically increased the need to ensure that people in the military services and their families had access to appropriate treatment and support. Information about programs in the district branches, university programs, and treatment resources was collected nationally and distributed in a variety of ways, particularly through the Public Affairs Network in the district branches. Younger and older members in the reserves were called to active duty to reinforce services to the military, which affected their lives and those of their families in various ways. Other members increased their workloads to bridge the gaps left by those on active duty.

The Board has been particularly mindful of fiscal constraints imposed by the general economic climate on APA members and the Association. Your Treasurer will report to you in greater detail about the Association's finances.

The Board has dealt with many serious and complex matters at its meetings in May, June, September, and December 1990 and in March 1991. Contributing significantly to the agenda for the Board and assisting in the identification, organization, and synthesis of options for

the Association were the reports of the Assembly, Joint Reference Committee, joint commissions (government relations and public affairs), commissions (AIDS, judicial action, and subspecialization), and ad hoc committees established to address major issues in a timely fashion. A portion of each Board meeting was spent discussing policy issues and developing strategies to enhance the field of psychiatry and to assist members, patients, and their families.

Membership Changes

As of Jan. 1, 1991, the membership was 36,918, which is 710 (2%) more members than in 1990.

The category of Medical Student Membership was created in 1984, and these members have increased from 208 in early 1985 to 796 as of April 1, 1991. To encourage them to join APA, the membership this year passed amendments to the APA Constitution and Bylaws to set a one-time fee for medical students, rather than annual dues, and to exempt them from having to belong to a district branch until they graduate from medical school.

Of the various membership classes, the Member-in-Training category has had the largest increase in membership, from 1,378 in 1975 to 5,760 in January 1991. They now constitute 15.6% of the total membership and are the greatest source of new General Members. These residents are significantly involved in the activities and components of the Association; there is now a voting Member-in-Training Trustee and nonvoting Member-in-Training Trustee-Elect on the Board and an area representative and deputy representative in each of the seven area councils. The Committee of Residents and Fellows and the resident fellowship programs continue to have representatives on the Board. The needs and interests of younger psychiatrists beyond residency are focused in the Committee of Young Psychiatrists, which is charged to direct activities to identify these APA members, to assess their interests and needs, and to make recommendations as to how the Association can best serve them. The committee is extensively involved in the activities of the American Medical Association (AMA) Section Council on Psychiatry and sends a delegate and an alternate to the annual and interim meetings of the AMA Young Physicians Section. In addition, APA has a young physician delegate and alternate delegate in the AMA House of Delegates.

Membership and Fiscal Policies

In response to member concerns about rising APA dues and the changing demographics of APA membership, the Ad Hoc Committee on Membership and Fiscal Policies was established in December 1989 to investigate trends in APA membership and dues revenue and to consider two initiatives from the Assembly requesting that APA dues be frozen and that the granting of Life status as determined by the present formula (i.e., when the sum of a member's age and years of active membership is 95) be separated from the granting of a dues exemption.

Members of the ad hoc committee represented the Board, the Assembly, the Committee on Membership, and residents. APA's Office of Membership and a special staff consultant with necessary expertise assisted in the development and analysis of a wide range of pertinent data. Reports of the ad hoc committee were widely distributed to the district branches, the Assembly, and the Board and were discussed at meetings of the seven area councils, the Assembly, and the Board.

A number of trends were found that suggested a slower rate of growth in dues income in the future, primarily stabilization of the number of new members and rapid growth in the number of members who are becoming dues exempt. These trends, coupled with pressure to keep APA dues increases in line with inflation, would seriously hamper the ability of the Association to fund programs desired by the membership and forced on the field by outside pressures. In addition to fiscal austerity, revisions of fiscal and dues policies were needed to improve member retention. The greatest problems in membership retention were found in the district branches with the highest local dues; thus, it will be important for district branches to follow the national principles in establishing their dues.

The Board agreed that any change in the dues structure would reflect the ability of the average member to pay, i.e., dues should be phased in for younger members and phased out for senior members. The current three-step phase-in will be replaced with a revenue-neutral seven-step structure, beginning with the 1992 dues year.

The 1992 ballot will include amendments to permit charging new Life members modified dues while retaining the dues-exempt status of members who achieved Life status before 1993. The APA Constitution and Bylaws does provide for charging non-dues-paying members an annual communications fee for the *American Journal of Psychiatry*.

One of the most valuable features of the work of the ad hoc committee was the establishment of planning mechanisms, a time frame for longer-range budgetary planning, and yearly monitoring of the guidelines.

Member Benefits

In December 1990, the Board voted to designate the APA Purchasing Group, Inc., to replace the Committee on Insurance in making decisions about APA-sponsored insurance programs. The Board of Directors of the APA Purchasing Group held its first meeting in January 1991. The Board of Directors will have fiduciary and administrative responsibilities and oversee the work of related components. Several members of the Committee on Insurance will continue as directors with staggered terms, and the board has three members more than the committee. APA will appoint the members of the board in keeping with criteria approved by the APA Board of Trustees, which specify representatives of the Assembly, different geographic areas, younger members, and purchasers of the insurance.

Two major innovations were introduced in the 1991 renewal of the Professional Liability Insurance Program. Insured members with histories of significant claims will receive rate increases based on these experiences. The "experience rate" structure is designed to offset the costs of adverse selection of higher-risk members into the APA program, which has increased the basic rate beyond the levels of more selective commercial competitors. The program is also introducing a "claims made" option on a pilot basis in six states and the District of Columbia. The new option is designed to serve members who select "claims made" policies to cut current-year insurance premiums. The program continues to offer the enhanced protection provided by an "occurrence" policy in 49 states.

Because of the experience-rate program and the leveling off in the

growth of claims, the Professional Liability Insurance Program was able to keep its increase in the basic rate to 1% nationwide. This follows an average rate decrease of 3.5% nationwide on May 1, 1990. Seventeen states had no increases in 1991, and eight states had rate decreases based on their loss experience.

The catastrophic health insurance program was adopted after continuing losses in the APA-sponsored health insurance program for members. Now in its second year, the program offers a revised and reduced benefit structure and has a new rating procedure. Although participation has fallen, the program now appears to be financially stable, and the basic premium increased only 10% for 1991—well below the rate of increase in most commercial health insurance premiums.

Public Affairs

In 1990 and 1991, the Joint Commission on Public Affairs and the supporting Division of Public Affairs set new records in the 5-year "Let's Talk About Mental Illnesses" campaign, now in its fourth year. The campaign, the most ambitious public education effort ever mounted by the Association, seeks to heighten public awareness of mental illnesses and the effectiveness of psychiatric treatment. Its centerpiece is a series of three public education films: "The Panic Prison," "Faces of Anxiety," and "Depression: The Storm Within." Each 30-minute film features a psychiatrist and real patients. Production of the series was supported by an unrestricted educational grant from the Upjohn Company. From May 1990 through April 1991, the first two films were seen by more than 2 million people. The depression film goes into circulation in May 1991. Most of the viewers who watched the panic and anxiety films saw them on the Learning Channel and other outlets, including several state public broadcasting systems. The second largest number of viewers saw the films through free loans from Modern Talking Picture Service. Through these loans, 132,082 persons saw the films, primarily in classrooms and other organized settings. The Division of Public Affairs predicts that the 2 million audience will more than double by May 1992.

The Hometown Radio Interviews program again broke records: 170 million "audience impressions" resulted from radio interviews released during the annual meeting and again during Mental Illness Awareness Week.

The outreach to other physicians has also been successful. The popular workshop "Panic Disorders: Diagnosis, Recognition and Treatment" has been recommended to local chapters of the American College of Emergency Physicians with the suggestion that they call APA district branches and Upjohn medical and science liaisons to arrange local workshops. An Upjohn grant paid for development of the workshops and an active exhibit program that sent APA exhibits to more than 30 meetings of physicians and allied health professionals during the year.

In lieu of the biennial Public Affairs Institute originally set for February 1991, the Division of Public Affairs instead held "hands-on" public affairs workshops for district branch public affairs representatives during the spring 1991 area council meetings. In its continued development of the Public Affairs Network, the division strengthened and expanded its newsletter, *Network News*, combining it with the Newsletter Editors Feature Service. We look forward to 1992 and a combined public affairs and state legislative affairs conference.

Government Affairs

This report spans the end of the second session of the 101st Congress and the beginning of the first session of the 102nd Congress, a period marked by two major developments that affect mental care: the resolution in 1990, after a bitter struggle, of a 5-year deficit reduction plan, which has potentially profound consequences for health care funding, and the growing interest of the 102nd Congress in developing a framework for improving access to health care and insurance by the 32 million uninsured and underinsured Americans.

The current proposals range from reform of small-group health insurance coverage to implementation of a Canadian-style national health care single-payer system. Most of the bills introduced thus far in the 102nd Congress include utilization limits for inpatient and out-

patient treatment for mental disorders but not other illnesses. One bill would not require any coverage of mental disorders.

Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) appropriations. Despite the deficit reduction pressures at the end of the 101st Congress, APA was again successful in achieving substantial increases in ADAMHA funding for fiscal 1991. The total ADAMHA appropriation for fiscal 1991 was \$2.9 billion, a 9.6% increase over the fiscal 1990 funding of \$2.65 billion. The National Institutes of Health also received a 9.6% funding increase over its fiscal 1990 level. The total National Institute of Mental Health funding of \$535.4 million was a 15.6% increase over fiscal 1990.

Americans With Disabilities Act. Public Law 101-336 promotes the civil rights of 43 million citizens with disabilities, which include mental illness because APA opposed legislative efforts to exclude the mentally ill from the protection of this landmark legislation.

CHAMPUS. APA has continued to oppose the proposal to establish a demonstration program within the U.S. Department of the Army to train clinical psychologists to prescribe drugs, and more than 30 members of the House of Representatives cosigned a letter authored by Congressman Ronald Machtley that urged Congressman Beverly Byron, chairperson of the House Subcommittee on Military Personnel and Compensation, to hold hearings on the program. The letter stated that "the prescribing of potentially dangerous psychoactive medications should be limited to those professionals who have the proper medical education and residency training."

Immigration. The 101st Congress cleared for the President a major revision of U.S. immigration laws. APA, specifically cited in the conference report, won changes that will mean would-be immigrants will no longer be excluded solely because of mental disorders (exclusion on the basis of physical or mental disorders was linked carefully to behavior rather than diagnosis), and homosexuality also was dropped as a reason for exclusion.

Mental Illness Awareness Week. The President signed into law a resolution designating the week of Oct. 7-13, 1990, as Mental Illness Awareness Week. APA marked the event with a daylong symposium on Capitol Hill, which was attended by dozens of members of Congress and key Congressional staff. Senator Paul Simon and Congressman Ron Wyden are the chief sponsors of the resolution in the Senate and House in the 102nd Congress.

Physician Payment Review Commission. APA learned that the Physician Payment Review Commission was planning to recommend that clinical psychologists and psychiatrists be reimbursed at the same rate for services they both provide, singling out clinical psychologists as the only nonphysician providers for which the commission was going to recommend payment equal to that received by their physician counterparts. Successful APA lobbying led to a revision, and the commission's 1991 report to Congress, released early in April, recommended that clinical psychologists retain their current classification in the U.S. code as nonphysician providers and receive an as yet undetermined percentage of the Medicare reimbursement to psychiatrists for services they both provide. While the recommendations regarding the role of nonphysician providers is a positive outcome for APA, the role of nonphysicians in the new Resource-Based Relative Value Scale Medicare fee schedule must still be considered by Congress and the Health Care Financing Administration.

Federal Legislative Institute. The 1991 Federal Legislative Institute, held March 10-12 in Washington, D.C., was a major success. Total attendance was 93, an all-time high. President Elissa P. Benedek, M.D., President-Elect Lawrence Hartmann, M.D., Speaker Edward Hanin, M.D., Speaker-Elect G. Thomas Pfahler, M.D., and Medical Director, Melvin Sabshin, M.D., participated in the presentations. The participants received panel briefings from key Congressional and executive branch staff on the role of nonphysicians in the delivery of mental health care, on managed care, and on government control in the practice of psychiatry. A dinner was held in honor of Senator Pete Domenici (R-N.M.), and he was given the Jacob Javits Award for his efforts on behalf of the mentally ill.

APA legislative representatives and area leaders visited 230 Congressional offices and met with members of Congress and their key health care aides. The APA delegations were well received and left behind a series of fact sheets outlining APA concerns on numerous federal issues.

Economic Affairs

The Ad Hoc Committee on Managed Care Issues, which was established by the Board in December 1989, identified a number of steps that could be taken rapidly and over a longer period. The ad hoc committee's charge was continued in June 1990. Also, the Committee on Managed Care was established in the Council on Economic Affairs in June. It held an organizational meeting in September 1990 and met again in January 1991.

APA has been developing a range of strategies, including guidance for state legislative and regulatory initiatives, data gathering, and education, including cost studies. The "Managed Care Survival Manual" is being written to educate members about the process of managed care and utilization review. Fact sheets on issues involving the economics of psychiatric practice and a quarterly newsletter, *Eco-Facts*, are available through our Office of Economic Affairs. Collection of medical necessity criteria used by managed care organizations has begun, and a criteria library is being developed in the Office of Economic Affairs. A managed care hot line, with a toll free number, was implemented so members could report problems and obtain answers to a variety of questions. Documented problems are being reviewed by the Committee on Managed Care. Staff is preparing the reviewed cases for presentation to managed care organizations so that the cases can be discussed with them and problems can be addressed. A managed care network is facilitating the flow of information between the district branches and the national office and the committee.

From the beginning, in addition to these initiatives, APA has been aware that litigation against managed care companies who engage in egregious practices detrimental to patients might be a component of the overall efforts.

Work Group on Codes and Reimbursements

In June 1990 the Board approved the policy that the Assembly review and vote on the codes APA proposes to the AMA for *Physicians' Current Procedural Terminology, 4th edition (CPT-4)*, and it also approved the mechanism set up by the Assembly and its Executive Committee to review the codes quickly and not delay the process. Consistent with the policy approved by the Board, the officers of the Assembly reviewed the recent vignettes describing the levels of service in the evaluation and management codes submitted to the AMA. Dr. Chester Schmidt, chairperson of the Work Group on Codes and Reimbursements, reported to the Board at its March 1991 meeting.

The 1992 CPT-4 will contain three new codes for interactive therapy: interactive psychiatric diagnostic review, interactive individual medical psychotherapy, and interactive group medical psychotherapy.

Dr. Tracy R. Gordy was appointed to the AMA CPT editorial panel in 1990. Dr. Gordy is the first psychiatrist to serve as a member of the 12-person panel, which is charged with the annual revisions to CPT-4.

Work Group on the Harvard Resource-Based Relative Value Scale

The APA Work Group on the Harvard Resource-Based Relative Value Scale Study, chaired by Dr. Donald Scherl, has been very active over the past year. Most notable is the work group's review and analysis of the phase II research conducted by Harvard University under the direction of William Hsiao, Ph.D.

The phase II work, published in a January 1991 report, holds good news for psychiatry and is a significant improvement over the phase I work. In summary, 1) the phase II values for psychiatric services are on average 10% higher than the phase I estimates; 2) the Harvard research confirms that the existing CPT codes do not capture the full range of psychiatric services and that new codes are warranted; and 3) the report acknowledges that patient characteristics, such as dangerousness or youthfulness, affect physician work and should be reflected in the reimbursement system.

While APA remains concerned about some of the methods used by the Hsiao study team at Harvard, the team did respond to the myriad of methodological questions and concerns raised by APA. The positive outcome will not hold for all practitioners in all geographic areas. While some psychiatrists will see increases in the Medicare fees, others will almost certainly see decreases—and this is especially so in areas in which fees are already above the national average.

Research

Practice guidelines (parameters). Noting a trend for the development of such guidelines by government agencies, the Board established the Work Group on Practice Parameters in March 1990 to make recommendations as to how APA could develop practice guidelines and to explore and suggest a process for doing so. A forum on the topic was held in November 1990 in conjunction with the orientation sessions for district branch presidents-elect and staff and the fall Assembly. The Board, Assembly, Council on Psychiatric Services, and Joint Reference Committee heard reports from the work group and commented on its recommendations. The work group was then replaced by the Steering Committee on Practice Guidelines to oversee and coordinate their development under the Council on Research. The steering committee discussed the criteria for selection of APA's guideline topics and is working toward developing guidelines in 1991 in the following areas: inpatient evaluation, outpatient evaluation, eating disorders (anorexia and bulimia), and major depression. Practicing clinicians will be involved in the development of these guidelines, and knowledgeable scientists will have an opportunity for input.

The developmental process will include circulation of drafts for comment to individuals, components, the Assembly and district branches, other societies, and other relevant individuals and groups.

The steering committee hopes to obtain external funding to assist in refining its methods and developing guidelines in more difficult and complex areas of psychiatric practice over the next several months.

The AMA continues to use the term "practice parameters" and is very committed to working with specialty societies as they develop their own parameters/guidelines.

DSM activities. The Task Force on DSM-IV reminded the Board that the *DSM-IV Options Book* will be available in early summer 1991 and will include the range of options being considered for DSM-IV. The options book continues the systematic and open process that has been in place since the initiation of DSM-IV. Comments on the options being considered are both requested and encouraged.

A primary care version of DSM-IV, designed to improve the recognition and appropriate diagnosis of patients with mental disorders in primary care settings and to facilitate communication between psychiatrists and primary care physicians, is being developed. It will be compatible with DSM-IV and will be published after DSM-IV.

Resource Development

On Jan. 22, 1991, the American Psychiatric Foundation, Inc., was incorporated in the District of Columbia. The foundation's interim directors were unanimously approved by the APA Board of Trustees at its meeting in March 1991. The foundation will provide a focal point for expanded APA resource development activities and an opportunity to go beyond existing APA constituencies. In keeping with this innovative direction, the Board also approved the recommendations of the Resource Development Committee to create the APA pooled income fund, the Corporate Partners Program, and a donor recognition program.

"Fund for the Future—APA" promotions, which included a series of Board-approved solicitations of APA Life Members and Life Fellows, has resulted in more than \$100,000 in contributions. A special fund-raising initiative to increase the Foundations' Fund Prize endowment to \$100,000 also is underway.

Ms. Andrea Morgan is Director of the APA Office of Resource Development, which provides staff support to the Resource Development Committee and the American Psychiatric Foundation.

Ethics

Educational programs continued to help members learn about the new procedures for handling complaints of unethical conduct that were implemented in October 1989. Sessions on ethics procedures, including one for district branch staff, were held during the orientation for district branch presidents-elect and staff and new Assembly members in November 1990. Through funds provided by the Board, consultation services were provided by Ms. JoAnn Macbeth of Onck, Klein, & Farr and by Ms. Carol Davis, who staffs the Ethics Commit-

tee. "How to Hold a Hearing," a videotape, is available free of charge from the Medical Director's Office.

As recommended by the Assembly, the Board approved a mechanism to enable and fund district branches' participation in hearings of their cases by the Ethics Appeal Board. The Board urged the district branches to participate by speakerphone as often as possible to minimize travel costs.

The Board voted to expel several members because of ethical violations. The names of expelled members are printed in *Psychiatric News*, and federal law requires that all suspensions and expulsions be reported to the National Practitioner Data Bank.

The Ad Hoc Committee to Study the Composition and Procedures of the Ethics Appeal Board met in March and will report to the Board in June 1991.

The Subcommittee on Education of Psychiatrists on Ethical Issues has produced two videotapes: "Sexual Activity with Patients" and "Reporting Complaints of Unethical Conduct." The videotapes are available from the American Psychiatric Press at a cost of \$30 to district branches and \$100 to others. The Board voted to discharge the subcommittee with appreciation after it presents a workshop at the 1991 annual meeting.

Judicial Affairs

In June 1990, the Board authorized paying the California Psychiatric Association (Area VI) \$21,342 to help defray its costs in *CAPP v. Rank*. The money was drawn from the budget of the Commission on Judicial Action and the Board's contingency fund. In July 1990 *Psychiatric News* reported the decision in favor of the psychologists' position and its implications. The Board also made a final contribution of \$44,980 to the California Psychiatric Association in March 1991, as one-half of the costs borne by Area VI related to a lawsuit subsequent to the *CAPP v. Rank* decision.

Subspecialization

An ad hoc committee worked for several years in concert with appropriate APA components to develop recommendations for criteria to determine when a group of psychiatrists with special interests and types of practice is ready for added qualifications in their field and a process by which APA can develop recommendations to the American Board of Psychiatry and Neurology (ABPN) when these groups apply to the ABPN. These criteria and the process were approved by the Assembly in May and by the Board in June 1990. The Board discharged the ad hoc committee with appreciation and established the Commission on Subspecialization. During the past year, as approved by the Assembly and the Board, APA recommended to the ABPN that it establish a process for granting added qualifications in addiction psychiatry. The Commission on Subspecialization met in January 1991 to review an application from forensic psychiatrists and held a hearing with some of their representatives. The commission found that the 10 criteria had been met. The Assembly will be discussing the commission's report in May and will make recommendations to the Board for consideration at its meeting in June 1991. The commission has recently received an application from a consortium of consultation-liaison psychiatrists and is studying it.

Internal and External Liaison

Communication among the district branches and between them and the national organization is increasingly important. The district branches are gathering information about some major economic issues and have considerable leadership and expertise to share nationally and with each other. Each fall and during the annual meeting their presidents-elect are convened to discuss mutual concerns and to learn how the national elected leadership and staff can assist them. Almost 60 of the 76 district branches have paid staff with a wide range of expertise to enhance local functioning and improve interactions with the national association. Every other year national funds are made available for transportation of one district branch staff member to an orientation in conjunction with the fall Assembly.

APA has many vital interactive and collaborative relationships with related organizations in psychiatry and all of medicine, with other

mental health disciplines, and with citizen patient advocacy groups. These relationships are implemented in a variety of ways. For example, representatives of allied groups hold meetings in concert with our annual meetings and annual Institutes on Hospital & Community Psychiatry, and their presence is recognized at those meetings. APA sends representatives to both social gatherings and working meetings of allied organizations. There is a trend toward special interests and expertise, and many psychiatrists belong to organizations besides APA. Ways to give them greater voice in the development of APA policies and to involve them in ways that use their particular expertise are being explored. The Ad Hoc Committee on Liaisons identified over 80 allied groups and has been convening meetings with representatives of more than 20 of them who have expressed interest in meeting together to determine how they can be more actively involved in the Association and how the Association can provide information and services to them.

Every member of APA is welcome to attend any meeting of APA's components, except meetings of the Ethics Committee and Ethics Appeals Board or when a component goes into executive session. Your strong support is deeply appreciated; your recommendations for consideration by the Board or other components are most welcome.

Thank you for the privilege and honor of serving as your Secretary for the past 2 years. I look forward to working with you in the future!

SUMMARY OF ACTIONS

The actions of the Board of Trustees are grouped by topic, and the topics are arranged alphabetically. The date of each action is given in parentheses at the end of the action.

Addiction

1. Authorized APA cosponsorship of ADAMHA's Primary Care Provider/Substance Abuse Linkage Initiative, at no cost to APA (June 1990).

2. Authorized the Committee on Training and Education in Addiction Psychiatry, following established procedures and working in conjunction with the Medical Director's Office, to seek outside funding to support its ongoing work (June 1990).

3. Approved expressing APA's concern about the omission of detoxification from the basic package of benefits required for employer insurance programs in a report adopted by the AMA House of Delegates in June 1990, titled "Covering the Uninsured," which described a package of minimum health insurance benefits for all employer coverage (Dec. 1990).

Aging

1. Requested the Committee on Long-Term Care and Treatment for the Elderly (within the Council on Aging) and/or other appropriate components to assess the feasibility of APA's joining with the American Association of Retired Persons (AARP) in developing a model for coverage of long-term care that both organizations could support and that would adequately protect psychiatric patients and ex-patients; and asked the committee to develop, if feasible, a proposal for the Board's review that would provide a model long-term care policy which could be jointly supported by the two organizations (Dec. 1990).

2. Approved APA participation in the Coalition on Mental Health and Aging established by the AARP, without commitment of APA funds at this point (Dec. 1990).

3. Authorized the Task Force on Models of Practice in Geropsychiatry to seek \$5,000 in outside funding, following established procedures and working in conjunction with the Medical Director's Office, to support development of a publication on models of practice in geropsychiatry (Dec. 1990).

4. Approved the report of the Corresponding Task Force on Geriatric Psychiatry in the Public Mental Health Sector titled *State Mental Hospitals and the Elderly*, for publication as part of the APA task force report series (March 1991).

5. Authorized the Council on Aging to seek outside funding, following established procedures and working in conjunction with the

Medical Director's Office, for the development of a grant proposal to obtain funding for a consultant to APA who would provide staff assistance for activities related to the 1991 White House Conference on Aging (Sept. 1990).

6. Authorized APA's President to appoint an APA representative to the Presidential Advisory Board on the White House Conference on Aging; recommendations for the representative were submitted by the Council on Aging (Sept. 1990).

7. Allocated \$4,000 from the 1990 Board contingency fund to support a meeting of the Task Force on the White House Conference on Aging (Sept. 1990).

8. Authorized the Council on Aging to seek outside funding, following established procedures and working in conjunction with the Medical Director's Office, to support two APA-sponsored miniconferences before the 1991 White House Conference on Aging (Sept. 1990).

AIDS

1. Authorized the search for outside funding of AIDS education and policy efforts, following established procedures and in conjunction with the Medical Director's Office (March 1991).

2. Authorized the use of a New York State Department of Health analysis as a resource document to guide APA, as appropriate, on the issue of HIV-infected health care workers (March 1991).

3. Approved the revised "Interim Guidelines Regarding Psychiatrists Who Are HIV Infected" as an official APA position statement (Dec. 1990).

4. Approved the "Interim Guidelines for Occupational HIV Exposure Protocols and Protections" as an official APA position statement (Dec. 1990).

5. Approved the "Position Statement on HIV and Youth," contingent on the approval of the Assembly (March 1991).

American Board of Psychiatry and Neurology

1. Requested the Council on Medical Education and Career Development to develop strategies that APA can use for significantly increasing the number of international medical graduates, women, and underrepresented minorities who are certified, asking the council to report back to the Board in June 1991 (Dec. 1990).

2. Approved APA's removal of tables and other material that specifically differentiates American and international medical graduates when APA distributes or publishes information about performance on ABPN examinations; further, voted to begin a dialogue with the ABPN concerning sensitivity in the collection, analysis, and reporting of data (Dec. 1990).

3. Ratified an Executive Action taken by the President, Speaker, and Medical Director to approve the nominations of the following psychiatrists as candidates for the ABPN Committee on Certification in Child Psychiatry: Drs. Eugene Berensen, Mohammad Shafii, and Alayne Yates (March 1991).

4. Voted to nominate Drs. Sanford Finkel, Gary Gottlieb, and Dilip Jeste for the ABPN Committee on Added Qualifications in Geriatric Psychiatry (June 1990).

5. Approved forwarding the names of the following nominees for ABPN director, in this ranked order, to the ABPN: Drs. William McKinney, Stefan Stein, Eduardo Val, Sheldon Miller, and Renato Alarcon (June 1990).

6. Ratified the Executive Action taken by the President, Speaker, and Medical Director to renominate Dr. James Shore as a director of the ABPN (Sept. 1990).

7. Submitted to the AMA Section Council on Psychiatry the names submitted by the Ad Hoc Committee to Develop a Slate of Candidates for Election to the ABPN, but with the following changes: Dr. Eduardo Val would be ranked first, Dr. Henry Nasrallah would be second, Dr. Lindbergh Sata would be third, and the rest of the names would be listed in the same order in which they appear on the list (Dec. 1990).

8. Agreed to publicize in *Psychiatric News* and other appropriate publications, insofar as possible, the following information: a) the process used to nominate directors of the ABPN; b) the dates of examinations, geographic rotation of locations, and process used to select examiners for the ABPN part II examination; and c) the findings

of a survey of non-Board-certified psychiatrists conducted by the APA Task Force on Recertification (June 1990).

American Journal of Psychiatry

1. Reappointed Dr. Kenneth L. Davis to his second 4-year term as Associate Editor of the *American Journal of Psychiatry* (March 1991).
2. Appointed Drs. Gabrielle A. Carlson and David Spiegel to 4-year terms as Associate Editors of the *American Journal of Psychiatry*; their terms begin at the end of the 1991 annual meeting (March 1991).
3. Ratified an Executive Action taken by the President, Speaker, and Medical Director to implement an institutional subscription rate (initially set at \$85 per year) for the *American Journal of Psychiatry* (Sept. 1990).

American Medical Association

1. Regarding the "AMA Statement on HIV-Infected Physicians," noted that APA would like to persuade the AMA (in whatever ways it can) to at least replace the word "identifiable" with "significant" where appropriate; further, voted to request the AMA to expand the statement to include all life-threatening communicable infections, not just AIDS (March 1991).
2. Voted to accept procedures by which the Assembly will review and approve the CPT code proposals sent by APA to the CPT editorial board; further, voted that, if prompt action is necessary, the Assembly Executive Committee or the immediate past Speaker, Speaker, Speaker-Elect, and Recorder would act for the Assembly in this matter (June 1990).
3. Approved the following policy: "APA, through its components and AMA representatives, request that AMA, which wholly owns the CPT coding system, license the use of CPT coding solely for physicians' services, in accordance with its original intent" (Dec. 1990).
4. Authorized APA cosponsorship of the video teleconferences on the evaluation and treatment of depression by primary care physicians, with the understanding that APA will be actively involved in the substance of what is presented in the videotapes; further, authorized support from the Joint Commission on Public Affairs and the Division of Public Affairs as requested by the AMA (June 1990).
5. Agreed that the invitation from JAMA to Dr. Sabshin (and executive directors of other specialty organizations) to write an article on the theme "Caring for the Uninsured and Underinsured" for possible publication in a spring 1991 issue should be accepted; further, voted that, although this would not be an APA policy statement, Dr. Sabshin could request assistance from staff in the Division of Government Relations, the Office of Economic Affairs, and other staff offices and that Dr. Sabshin could list the names of those who worked with him as coauthors of this article (Sept. 1990).
6. Accepted the final report of the Ad Hoc Advisory Panel of the AMA/Specialty Society Practice Parameters Partnership, including the recommendations, the modifications to the "Attributes to Guide the Development of the Practice Parameters," and the self-assessment instrument for the evaluation of practice guidelines (Dec. 1990).
7. Requested that the AMA Section Council on Psychiatry support the appointment of a psychiatrist to the proposed AMA committee on telemedicine (June 1990).

American Psychiatric Press

1. Appointed Dr. Elissa Benedek to a 4-year term on the Board of Directors of the American Psychiatric Press, Inc. (May 1990).

Annual Meeting

1. Approved arrangements for holding the 1992 annual business meeting and forum on Sunday (rather than on Monday, as in previous years) immediately after the conclusion of the Assembly, as a pilot project (Sept. 1990, Dec. 1990, March 1991).
2. Approved the "Guidelines for Industry-Sponsored Symposia" (March 1991).
3. Authorized allocation of \$3,000 in the 1991 annual meeting budget for services for the hearing impaired (Sept. 1990).
4. Authorized the Committee on Psychological Aspects of Nuclear

Issues to seek \$3,650 in outside funding, following established procedures and working in conjunction with the Medical Director's Office, to support a symposium at the 1992 APA annual meeting (Dec. 1990).

5. Authorized the Committee on Telemedical Services to seek \$5,000 in outside funding, following established procedures and working in conjunction with the Medical Director's Office, for an exhibit at the 1992 annual meeting (Dec. 1990).
6. Authorized the Committee on Women, following established procedures and working in conjunction with the Medical Director's Office, to seek outside funding for a women's activity center at the 1991 annual meeting (Dec. 1990).

Awards

1. Approved changes to the eligibility requirements, criteria, and procedures of the Distinguished Service Award and altered the structure of the Distinguished Service Awards Committee (June 1990).
2. Approved the following recipients of the Distinguished Service Awards to be presented at the 1991 annual meeting: Dr. Clifford B. Robinowitz and David A. Hamburg for the individual awards and ADAMHA for the institutional award (Sept. 1990).
3. Established an annual award for human rights activities and referred this action to the Committee on Grants and Awards to ensure that all aspects of the award are in proper order; further, authorized the Council on International Affairs and the Committee on Human Rights to seek outside funding, following established procedures and working in conjunction with the Medical Director's Office, to cover the costs and honorarium (if any) for this award (Dec. 1990).
4. Initiated an interim procedure for reviewing the names of selected persons to receive awards and requested the Council on Internal Organization to provide a list to the Board of Trustees at its September 1990 meeting of the selected award winners who were asked to provide lectures during the 1991 annual meeting, with the understanding that no action was required of the Board after it received this list (the list was received by the Board at its September 1990 meeting) (June 1990).

Biopsychosocial Issues

1. Adopted the following statement as official APA policy: "Mental disorders, like many other disorders, have biopsychosocial components" (June 1990).
2. Voted to reaffirm and actively promulgate the following position: "It is essential to comprehensive, effective medical psychiatric treatment that biological, psychotherapeutic and psychosocial interventions be reimbursed, without limitations that discriminate solely on the basis of biological vs. nonbiological aspects of diagnosis or etiology, and that all advocacy by the APA and its components should work towards that ultimate objective" (June 1990).

Components—Discharged

1. *Constitutional components:* Ethics Committee's Subcommittee on Education of Psychiatrists on Ethical Issues (Dec. 1990).
2. *Board of Trustees components:* Ad Hoc Committee on Hospitalization of Adolescents (June 1990); Ad Hoc Committee on Membership and Fiscal Issues (not renewed in June 1990); Ad Hoc Committee on Subspecialization (June 1990); Work Group on Practice Guidelines (Sept. 1990); Board Committee on Insurance (Dec. 1990).
3. *Council on Economic Affairs:* Task Force on Future Trends in Private Insurance (discharged after the May 1991 meeting of the task force) (March 1991).
4. *Council on Psychiatric Services:* Committee on Alcoholism (June 1990); Committee on Drug Abuse (June 1990); Committee on Rehabilitation (March 1991); Task Force on SSI/SSDI (March 1991); Task Force on Psychiatric Services for Mentally Retarded and Developmentally Disabled Adults (March 1991); Committee on APA Liaison With the American Hospital Association (to be discharged once the new APA/AHA liaison structure is in place) (March 1991).
5. *Council on Research:* Task Force on Prevention Research (June 1990); Task Force to Study the Long-Term Effects of Lithium on the Kidney (Dec. 1990); Task Force on Benzodiazepine Dependency (Dec. 1990).

Components—Established

1. *Board of Trustees components*: Commission on Subspecialization (June 1990); Ad Hoc Committee on Conflicts of Interest (Dec. 1990).
2. *Council on Addiction Psychiatry*: Committee on Training and Education in Addiction Psychiatry (June 1990); Task Force on Criminalization/Decriminalization of Drugs (Dec. 1990); Task Force on Psychiatric Services for Addicted Patients (March 1991).
3. *Council on Children, Adolescents, and Their Families*: Task Force to Study the Use and Abuse of Psychiatric Hospitalization of Minors (Dec. 1990).
4. *Council on Economic Affairs*: Committee on Universal Access to Health Care (June 1990); Committee on Managed Care (June 1990).
5. *Council on International Affairs*: Task Force on APA Liaison With the World Psychiatric Association (June 1990).
6. *Council on Medical Education and Career Development*: Work Group on Recertification (March 1991).
7. *Council on Psychiatric Services*: Committee on Psychiatric Services for Mentally Retarded and Developmentally Disabled Persons (Dec. 1990); Committee on Disability and Rehabilitation (March 1991).
8. *Council on Research*: Steering Committee on Practice Guidelines (Sept. 1990).

Components—Modified

1. *Constitutional components*: Expanded the charge of the Budget Committee to include short-term fiscal planning (March 1991); revised the charge to the Joint Reference Committee to include serving as a clearinghouse for information flow between the Board and/or Assembly and the councils and commissions (Dec. 1990).
2. *Board of Trustees components*: Revised the charge to the Commission on AIDS (Sept. 1990); revised the charge of the Editorial Review Panel (Dec. 1990); approved changes in the structure of the Distinguished Service Awards Committee and adjusted the tenures of its members to provide for rotation (June 1990).
3. *Council on Economic Affairs*: Revised the charge to the Committee on Quality Assurance (June 1990); increased liaisons to the Committee on Managed Care, including liaisons from the Committee on Private Practice, the Committee of Young Psychiatrists, and one of the resident components or groups (June 1990).
4. *Council on National Affairs*: Revised the charge to the Council on National Affairs (Dec. 1990); revised the charge to the Committee of Asian-American Psychiatrists (Dec. 1990); revised the charge to the Committee of Black Psychiatrists (Dec. 1990); changed the name of the Committee on Foreign Medical Graduates to the Committee on International Medical Graduates (Dec. 1990).
5. *Council on Psychiatric Services*: Increased the membership of the Task Force on the Homeless Mentally Ill to include additional clinical experts (June 1990); changed the name of the Committee to Coordinate the Functions of the H&CP Service, Journal, and Institute to the Committee on the H&CP Service (Dec. 1990); revised the charge to the Committee on State and Community Psychiatry Systems (Dec. 1990); authorized appointing a psychiatrist from the U.S. Public Health Service as a consultant to the Committee on the Military (Dec. 1990); adjusted the tenures of the members of the Committee on Liaison With the American Hospital Association to begin and end on January 1 (June 1990) and subsequently authorized discharging the committee once the new liaison structure is in place (see also "Liaison Activities" section) (March 1991).

Components—Renewed

1. All of the following were renewed for 1 year, unless indicated otherwise: Ad Hoc Committee on the Annual Business Meeting and Forum (June 1990); Ad Hoc Committee to Develop a Slate of Candidates for Election to the ABPN (June 1990); Ad Hoc Committee on Legislation Affecting Quality of Care (June 1990); Ad Hoc Committee on Liaison Activities (June 1990); Ad Hoc Committee on Managed Care Issues (June 1990); Ad Hoc Committee to Plan for APA's Sesquicentennial (June 1990); Ad Hoc Committee for the Pilot Advocacy Project (June 1990); Ad Hoc Committee to Revise Procedures for Nominating the MITTE (June 1990); Task Force on Post-Residency Fellowship Training Programs (renewed for 2 years) (June 1990).

Education

1. Authorized the Committee on Medical Student Education to produce a one-page, self-mailing newsletter (to be called *Lucid Associations*) for APA Medical Student Members and medical school psychiatry clubs (June 1990).
2. Authorized the Committee on Medical Student Education, following established procedures and working in conjunction with the Medical Director's Office, to seek outside funding for two projects designed to enhance medical student recruitment: \$10,000 to produce the videotape "Why Psychiatry?" and \$6,500 to fund an exhibit (Sept. 1990).
3. Approved the "Policy Regarding Residency Fellowship Programs" (Dec. 1990).

Elections

1. Accepted the results of the 1990 election and postponed consideration of disposition of the ballots from the 1990 election until the Board meeting on May 13, 1990 (May 1990).
2. Authorized staff to destroy the ballots from the 1990 election immediately after the 1990 annual meeting (May 1990).
3. Changed the wording of section II.A.4.a. of the election guidelines to include fax documents in the limits on the number of letters candidates may write (June 1990).
4. Replaced the current Section II.A.5. of the Election Guidelines with the following wording: "Candidates are asked not to participate in any election-related publication or activity in which their opponents have not been given the same opportunity" (June 1990).
5. Approved changes to the procedures for nominating the Member-in-Training Trustee-Elect: a) standardizing materials submitted by residents to the Nominating Committee, b) soliciting nominations after the annual meeting (rather than in April), c) publicizing the request for nominations in the area councils, the Assembly, *Psychiatric News*, and the *Psychiatric Residents' Newsletter*, d) working closely with the American Association of Directors of Psychiatric Residency Training to encourage recommendations of residents, and e) changing the deadline for receipt of nominations from July 31 to August 15 (Sept. 1990, Dec. 1990).
6. Approved increasing the number of signatures required for nomination by petition to 400 for national office and 100 for area trustees and Member-in-Training Trustee-Elect; further, referred this action to the Committee on Constitution and Bylaws for preparation of any necessary amendments, requesting that these proposed amendments be presented to Board at its March 1991 meeting so that they could be read to the membership at the 1991 annual business meeting and placed on the 1992 ballot (Dec. 1990).

Ethics

1. Approved the "Criteria for Distribution of Financial Aid to District Branches to Assist with Implementation of the Revised 'Procedures for Handling Complaints of Unethical Conduct'" (June 1990).
2. Approved the following recommendations: a) that any district branch which has a case coming before the APA Ethics Appeals Board shall be given timely notification of the date of the appeals hearing, b) that a member of the original district branch hearing panel shall participate in that hearing, either in person or, at the discretion of the district branch, by speakerphone, c) that a district branch may waive this right of participation at its discretion, and d) that all costs for such participation shall be the responsibility of APA; further, voted to authorize spending \$15,700 of the 1991 Board of Trustees contingency fund for these activities, subject to review in March 1991, with the understanding that district branches will be urged to use the speakerphone as often as possible (Dec. 1990).
3. Ratified the Executive Action taken by the President, Speaker, and Acting Medical Director, Carolyn B. Robinowitz, to settle a lawsuit in an ethics case (Dec. 1990).
4. Authorized the mandatory reporting of expulsions and the discretionary reporting of suspensions to the National Practitioner Data Base (under paragraph 2.5 of the "Procedures for Handling Complaints of Unethical Conduct" section of APA's "The Principles of Medical Ethics With Annotations Especially Applicable to Psychiatry") when a mem-

ber who has been notified of a district branch's decision, as reviewed by the APA Ethics Committee, that the member has acted unethically and should be expelled or suspended appeals that decision to the Ethics Appeals Board but tenders his or her resignation from APA and the district branch before the appeal (Dec. 1990).

5. Agreed to the addition (for the next 2 or 3 years) of the following wording to notices of expulsions printed in *Psychiatric News*: "Federal law requires that all suspensions and expulsions be reported to the National Practitioner Data Bank" (Dec. 1990).

Fiscal Issues (see also "Resource Development")

1. Approved an APA 1991 budget of approximately \$24.4 million, representing an increase of more than \$400,000 (about 2%) over the 1990 budget and less than the projected inflation rate of 6%; further, created a special fund to collect revenues and approved several revenue-enhancing measures, including an average increase in dues of 4.65%, an increase of \$10 in annual meeting registration fees, a charge to Life Members and Fellows for subscriptions to the *American Journal of Psychiatry* (initially set at \$40 per year), and an institutional subscription rate for the *American Journal of Psychiatry* (initially set at \$85 per year) (Dec. 1990).

2. Approved the execution of any and all documents required to establish a loan package with a term of up to 3 years and an initial maximum borrowing limit of up to 6.5 million dollars per year, with the understanding that the borrowing limit might be revised in later years with the approval of the Board of Trustees (June 1990).

3. Fully authorized the following representatives to sign checks and withdrawal forms for appropriate fiscal institutions and to carry out other functions specified on regular signature cards used by institutions approved for handling APA funds: Dr. Mary Jane R. England, Treasurer; Dr. Carolyn B. Robinowitz, Deputy Medical Director; Dr. Jack W. White, Deputy Director for Business Administration; Mr. Robert M. Milanicz, Comptroller; and Ms. Joanne P. Robinson, Deputy Comptroller (June 1990).

4. Approved the establishment of appropriate bank accounts at Riggs National Bank of Washington, D.C. (Sept. 1990).

5. Approved a resolution authorizing and ratifying the actions taken by Ms. Joanne P. Robinson, Deputy Comptroller, for the Association (Sept. 1990).

6. Approved establishing an APA checking account at the Hibernia National Bank in New Orleans for cash and checking operations at the 1991 annual meeting (March 1991).

7. Approved the following monies to be spent from the Board's 1990 contingency fund: \$3,000 to support the Ad Hoc Committee on Legislation Affecting Quality of Care and \$10,500 to support the Work Group on Practice Parameters (June 1990).

8. Authorized the following from the Board of Trustees' 1991 contingency fund: up to \$30,000 to support continued work by legal counsel on litigation regarding managed care, with the understanding that if APA files a suit, this money will be repaid from assessments made to support the suit; up to \$5,000 to support APA's participation in the Joint Commission on Interprofessional Affairs conference on interdisciplinary collaboration in mental health (see "Liaison Activities" section), noting that some of the money may come from the Board's 1992 contingency fund; and \$15,700 for attendance of district branch ethics committee representatives at meetings of the Ethics Appeals Board, subject to review at the March 1991 meeting of the Board (Dec. 1990).

9. Allocated the remaining \$4,058 in the Board's 1991 contingency fund to support the expanded functions of the Budget Committee; this is a portion of the \$6,000 needed to carry out these functions, and the Board agreed to look further for the additional \$1,942 (March 1991).

10. Approved payment of \$21,342 to the California Psychiatric Association to help defray its costs in *CAPP v. Rank*, with the understanding that \$5,000 would come from the budget of the Commission on Judicial Action and \$16,342 would come from the 1990 Board contingency fund (June 1990, Dec. 1990).

11. As reported out of executive session, agreed to contribute \$44,980.42 (one-half of the outstanding balance) toward the costs related to a lawsuit subsequent to the *CAPP v. Rank* decision, with the understanding that this would be the final financial contribution from APA with respect to this case (March 1991).

12. Approved extending the dues amnesty (to forgive APA and district branch dues for members wishing to rejoin in 1990) through 1991, with the understanding that the amnesty would apply only to members who owed dues before 1988 (Dec. 1990).

13. Approved the following principle and activities with respect to the district branches: "District branches should be part of the solution [to members' concerns about high dues], and the APA should provide assistance to the district branches in analyzing and implementing dues policies that parallel the recommendations of the [Ad Hoc Committee's] report" (June 1990).

14. Voted not to institute a new category of dues for part-time practitioners and directed the Committee on Membership to re-emphasize to the district branches the existing guidelines for dues relief (waiver or reduction) (June 1990).

15. Approved several policies that would phase out dues for APA members achieving Life Member/Fellow status (two-thirds dues for the first 5 years, one-third for the second 5 years, and a communications fee thereafter); voted that existing APA Life Members/Fellows would be charged the communications fee beginning with the 1992 dues year; and voted to refer this issue to the Committee on Constitution and Bylaws for review and determination of whether any changes to the APA Constitution and Bylaws were necessary to implement these policies (June 1990).

16. Approved offering the option of lump-sum dues payments to the membership beginning in the fall of 1991, subject to the concurrence of the Budget Committee; further, approved procedures for implementing and administering lump-sum dues (June 1990, Dec. 1990).

17. Approved implementing the replacement of the current three-step phase-in of dues with the revenue-neutral seven-step structure, leading to the highest rate in the 8th year of membership (as approved by the Board in June 1990), beginning with the 1992 dues year (Dec. 1990).

18. Approved initially setting the one-time fee for Medical Student Members at \$25 and amended the "Operations Manual of the Board of Trustees" to indicate that acceptance of medical student membership in APA would be handled administratively by the Office of Membership, in consultation with the Committee on Membership as appropriate (Dec. 1990).

19. Authorized transfer of \$220 from APA dues to the National Psychiatric Society to permit a member of that district branch to become a Member-at-Large in APA (name on file) (Dec. 1990).

20. Allocated \$10,500 from the Board's contingency fund to support the activities of the Work Group on Practice Parameters for the 1990 budget year, with the understanding that a request for future funding would be made through the regular budget process (June 1990).

21. Approved expanding the functions of the Budget Committee to include short-term financial planning, with a major goal of building liquid reserves (March 1991).

Governance

1. Approved the request of the Committee on Constitution and Bylaws that, whenever feasible, the chairperson or a member of the Committee on Constitution and Bylaws be included in any substantive discussion by a component that might lead to changes requiring amendment(s) of the Constitution or Bylaws (Dec. 1990).

2. Approved amendments to Chapters 1.13 and 8.6 of the Bylaws, as recommended by the Committee on Constitution and Bylaws, for reading to the membership at the 1991 annual business meeting; for placement on the 1992 ballot; these amendments would permit charging new Life members modified dues and would retain the dues-exempt status of members who achieved Life status before 1973 (Dec. 1990).

3. Approved an amendment to Chapter 6.5 of the Bylaws, for reading to the membership at the 1991 annual meeting and for placement on the 1992 ballot; this amendment would expand the Nominating Committee to include a representative of a minority or underrepresented group (March 1991).

4. Approved an amendment to Chapter 9.1 of the APA Bylaws, for reading to the membership at the 1991 annual meeting and for placement on the 1992 ballot; this amendment would increase the number of signatures required for nomination by petition (March 1991).

5. Established a group to study the composition and procedures of the Ethics Appeals Board; further, decided that the membership of

this study group should include representatives from the Assembly, the Board of Trustees, and the Ethics Committee (Sept. 1990).

6. Authorized preparation of a document that describes fiduciary responsibilities and consequences of breaches of fiduciary duty, to be used for orientation of new Board members each June and, if appropriate, for orientation of district branch presidents-elect each November (March 1991).

7. Approved renaming the "Joint Reference Committee New Component Fund" the "Joint Reference Committee Contingency Fund" (June 1990).

8. Authorized the Medical Director (or his designee), in consultation with legal counsel, to settle claims against the Association that do not have significant policy implications for amounts up to \$25,000 and required the Medical Director to make a postaudit report of expenditures to the Board (March 1991).

9. Voted to waive policy to fund the Member-in-Training Trustee-Elect's attendance at meetings of the Assembly Committee of Area Member-in-Training Representatives and provided \$800 from the 1990 Board contingency fund to support this liaison activity for the balance of 1990, with the understanding that this funding would be included in the regular budget process in future years (June 1990).

10. Authorized the Medical Director to seek outside funding to support residents' involvement in governance activities during the 1991 annual meeting (June 1990).

11. Waived for 1 year the policy in the operations manual that prohibits reimbursement of members for attendance at APA annual meetings, to permit national funds to be used to support Assembly Member-in-Training area representatives' attendance at the May 1991 Assembly, with the understanding that up to \$6,000 would come from the Assembly Executive Committee's operating fund; agreed to assist in finding additional money for this purpose; further, referred to the Budget Committee and the Committee of Residents the overall issue of finding funds to support attendance of Members-in-Training in the governance structure at meetings held during the APA annual meeting (Dec. 1990).

12. Authorized preparation of an amendment that would add a representative from a minority or underrepresented group to the constitutional Nominating Committee; further, referred this action to the Committee on Constitution and Bylaws and requested that committee to prepare wording for one or more amendments to be read at the 1991 annual business meeting for placement on the 1992 ballot (Dec. 1990).

13. Approved a waiver of current policy to permit Dr. Allan Tasman to be reappointed to serve an additional year (through May 1992) as a member and chairperson of the Scientific Program Committee (May 1990).

14. Approved a waiver of current policy to permit Drs. Gordon Strauss and Kenneth Tardiff to be reappointed to serve an additional year (through May 1991) as members, and Dr. Strauss as chairperson, of the Steering Committee for the Psychiatric Knowledge and Skills Self-Assessment Program VI (May 1990).

15. Ratified the Executive Action taken by the President, Speaker, and Medical Director to waive current policy to enable Dr. Dave Davis to be reappointed to the Committee of American Indian/Alaskan Native Psychiatrists (Sept. 1990).

16. Approved waiving current policy on tenure for council membership, as stated in the operations manual, for 1 year to enable Dr. Hartmann to reappoint Dr. Jerald Kay to serve an additional year (through May 1992) as chairperson and member of the Council on Medical Education and Career Development (March 1991).

17. Asked the Budget Committee to explore the feasibility of increasing the number of members on the Scientific Program Committee for the 1992-1993 appointment cycle (Dec. 1990).

18. Voted that chairpersons of joint commissions shall be appointed to 1-year terms, with the understanding that they may serve no more than 6 consecutive years in that position (March 1991).

Government Relations

1. Endorsed additional federal requirements for health warnings in advertisements for alcoholic beverages (June 1990).

2. Voted to continue to support establishment of APA-sponsored postgraduate fellowships in public policy and government affairs; fur-

ther, voted to authorize the Medical Director to explore potential sources of outside funding for this program (June 1990).

3. Authorized investigation of the possibility of a lawsuit against the U.S. Department of Health and Human Services for its refusal to establish Medicare criteria which would ensure that a psychologist receiving direct payment will consult with a physician when treating a patient; further, authorized using the Executive Action mechanism to approve filing such a suit, if deemed appropriate (June 1990).

4. Requested that appropriate APA staff and components seek collaboration and coordination with patient advocacy groups concerning prescribing privileges for psychologists in the military services (June 1990).

5. Charged the Ad Hoc Committee on Legislation Affecting Quality of Care to gather data on issues related to hospital bylaws and state statutes regarding psychologist privileges and to work with the Joint Commission on Government Relations and the Joint Commission on Public Affairs to develop an appropriate legislative strategy; further, allocated \$3,000 from the Board contingency fund to support its activities (June 1990).

6. Instructed the Division of Government Relations to acquaint appropriate Congressional committees with the Assembly's support of RU486 and to encourage state legislators to support research on RU486 in their states (June 1990).

7. Authorized an expenditure of up to \$40,000 in the 1990 budget to explore the feasibility of state legislative or regulatory action to address quality of care concerns with respect to the scope of practice of various mental health providers (Sept. 1990).

8. Ratified an Executive Action taken by the President, Speaker, and Acting Medical Director, Dr. Carolyn B. Robinowitz, authorizing communication with district branches and granting permission to use an updated survey instrument in the annual survey to determine state activities involving the Comprehensive Planning Act (Public Law 99-660) (Dec. 1990).

9. Agreed to support an AMA resolution endorsing national efforts to restore full deductibility of interest on education loans (June 1990).

10. Approved specific approaches for alleviating the burdens of student loans, as presented in an action paper from the Assembly Committee of Area Member-in-Training Representatives, and requested the Joint Commission on Government Relations to develop, implement, and coordinate a unified strategy to work toward eliminating the financial burdens of physicians-in-training (Dec. 1990).

11. Approved sending to all APA Members-in-Training and interested medical students a memorandum prepared by the Division of Government Relations in response to the Assembly's request for assistance in alleviating student indebtedness (Dec. 1990).

12. Endorsed the "Statement Concerning Psychiatric Services in the Veterans Administration" (June 1990).

Homelessness

1. Approved for publication the second interim report of the Task Force on the Homeless Mentally Ill, titled "Homeless Families and Children: A Psychiatric Perspective" (March 1991).

2. Endorsed the following statement: "The presence of homeless people in America, especially those who are suffering from mental illness, is unacceptable. The American Psychiatric Association must continue to develop strategies and advocate efforts to correct this tragic spectacle" (June 1990).

Hospital and Community Psychiatry

1. Reappointed Drs. Magda Campbell and James Shore to an additional 4-year term each on the *H&CP* Editorial Board (March 1991).

2. Appointed Dr. Stuart Keill to a 4-year term on the *H&CP* Editorial Board (March 1991).

3. Changed the schedule of the Institute on Hospital & Community Psychiatry so that the program, rather than beginning on Sunday and running through Thursday, begins on Friday and runs through Tuesday, with the understanding that this new schedule would become effective in 1992 if technical details could be renegotiated (June 1990).

4. Approved an increase in fees for industry-sponsored symposia at the Institute on Hospital & Community Psychiatry, beginning in 1991 (March 1991).

Impaired Physicians

1. Authorized APA to send a letter to the AMA indicating endorsement and support of the implementation of an AMA resolution calling for adequate funding and maintenance of the AMA's impaired physician program, but only if there appears to be a diminution of interest or effort by the AMA in this program in the near future (June 1990).
2. Endorsed the "Guidelines to District Branch Impaired Physician Committees" (Dec. 1990).

Insurance, Member

1. Appointed the members of the Board Committee on Insurance to the Board of Directors of the APA Purchasing Group, Inc., and decided that the members of this board will serve 3-year terms, except for these original directors, whose terms will vary, as determined by lot, so that the expiration of terms will be staggered; further, agreed that no member will be reappointed to the Board of Directors of the APA Purchasing Group if she or he has served 8 or more consecutive years on the Board Committee on Insurance or the APA Purchasing Group (Dec. 1990).
2. Authorized the Board Committee on Insurance or its successor to a) serve as the fiduciary for the Insurance and Group Insurance Trusts, b) act as the representative of the insureds in selecting and supervising insurance administrators, insurance carriers, and "fronting" insurers, c) approve changes in the design and coverage limitations of APA-sponsored policies, d) oversee the work of the Life, Accident, and Health Committee and the Risk Management Committee, e) provide liaison with APA-owned captive insurers who share risk within the program, and f) present an annual report on insurance program developments to the Board of Trustees and the Assembly (Dec. 1990).
3. Authorized the Board Committee on Insurance or its successor to manage the APA programs for professional liability insurance and group insurance in such a way as to provide for the needs of insured members; voted to authorize the committee to design and sponsor, or purchase, insurance programs that cover as wide a spectrum of members as possible without rendering the insurance program financially unsound; and permitted the committee to approve different premiums to different groups of members based on the risks presented by each group (Dec. 1990).
4. Authorized the President to appoint three additional members to the Board Committee on Insurance, using the criteria for membership set forth in the operations manual (Dec. 1990).
5. Approved a series of resolutions providing indemnification of members involved in the oversight of the APA-sponsored insurance program (Dec. 1990).
6. Endorsed the offering of "prior acts" coverage for APA's current professional liability insurance to members who transfer from claims-made malpractice policies into the APA-sponsored insurance program (June 1990).

International Affairs

1. Endorsed the "Position Statement on Apartheid" as a report of the Committee on Human Rights (March 1991).
2. Authorized the Task Force on Conflict Resolution to seek outside funding, following established procedures and working in conjunction with the Medical Director's Office, to support the task force's study on conflict resolution (Dec. 1990).
3. Authorized the Council on International Affairs to seek outside funding, following established procedures and working in conjunction with the Medical Director's Office, to support an invitational conference of American psychiatrists and Eastern European participants, which would be held within the next 2 years (Sept. 1990).
4. Agreed that the official joint meeting between APA and the Royal College of Psychiatrists could be substituted for APA participation in the Oct. 21-23, 1992, European conference (Sept. 1990).
5. Discontinued the routine scheduling of biennial joint meetings with psychiatric associations of other countries, unless additional staffing is provided in support of such ventures (Dec. 1990).
6. Authorized APA's exploration, initially by staff in consultation with the Council on International Affairs, to work, as is deemed ap-

propriate, with the Citizens for a Free Kuwait to help plan future mental health services in Kuwait (Dec. 1990).

7. Authorized the transmission of an official communique to the World Psychiatric Association (WPA) about the psychiatric situation on the island of Leros (Dec. 1990).

8. Authorized the President to write letters of inquiry to appropriate U.S. governmental agencies offering APA's assistance in any organized effort to meet the mental health needs of Americans involved in the Middle East crisis (Sept. 1990).

9. In conjunction with the preceding action, authorized APA and the district branches, working in conjunction with the American Academy of Child and Adolescent Psychiatry, to try to stimulate local efforts, including the volunteer work by psychiatrists, to assist families, children, adolescents, and other groups because mental health clinics and other military facilities might be overburdened (Sept. 1990).

10. Authorized APA to join the Sub-Saharan Africa Journal Distribution Program of the American Association for the Advancement of Science by contributing to libraries in Africa subscriptions to the *American Journal of Psychiatry* and the *H&CP* journal (June 1990).

11. Approved the following as APA's requirements for relating to Soviet psychiatry: a) exhibited reform in the leadership of Soviet psychiatry, b) public acknowledgment of past psychiatric abuse by the Soviet government, c) improvement in the Soviet mental health law, d) discontinuation of abuses associated with the psychiatric registry, e) rehabilitation and compensation for victims of psychiatric abuse and their families, f) establishment of a functioning psychiatric ethics panel within the All Union Society of Psychiatrists and Narcologists, and g) collaboration with the newly emerging Independent Psychiatric Association; further, approved this agenda as a task force report (Dec. 1990).

12. Adopted a policy stating that individuals or committees who represent APA need to consult with the Council on International Affairs before a) inviting foreign psychiatrists or guests to attend meetings of APA as guests of the Association, b) bestowing lectureship awards or other honors on foreign psychiatrists or guests, and c) making statements on behalf of APA in respect to the ethical standing of any foreign psychiatrists, either as individuals or as a group (March 1991).

13. Voted that APA contact the WPA to indicate APA's displeasure over the cancellation of the visit to the U.S.S.R. by the review committee's representatives; voted to urge the WPA to take the steps necessary to conduct the visit in the near future; and voted to indicate that, if the WPA fails to do so, APA intends to propose suspension of the conditional membership of the All Union Society in the WPA (March 1991).

Judicial Activities

1. Contributed, with the help of the Medical Director, a small amount of money to an educational and legal fund for the Southern California Psychiatric Society, as symbolic of the Board's concern for the officers and the district branch, which had been served an injunction by the Federal Trade Commission (Sept. 1990).

2. Approved issuing a statement supporting the plaintiffs' position in *Doe v. O'Connor* (June 1990).

3. Ratified an Executive Action taken by the President, Speaker, and Acting Medical Director, Dr. Carolyn B. Robinowitz, to authorize APA to sign onto an amicus brief in *Visser v. Taylor* (March 1991).

4. Approved payment of up to \$5,000 on a matching basis to the New York State Psychiatric Association, Inc., for the cost of an amicus curiae brief in *Savastano v. Nurnberg*, a case in the New York Court of Appeals (June 1990).

5. Authorized the chairperson of the Commission on Judicial Action, in consultation with APA legal counsel, to approve APA's participation as a coamicus in the American College of Obstetricians and Gynecologists brief in *York v. Sullivan*, on the condition that the brief be written with consistent with APA policy; further, authorized a contribution of up to \$5,000 to defray the cost of the brief (June 1990).

6. Voted that APA would not participate as a coamicus in *New York Society of Surgeons v. Axelrod*, after a report in executive session by Dr. Zonana, chairperson of the Commission on Judicial Action, and a long discussion that included input from the Executive Council (Dec. 1990).

7. Approved the recommendation of the Commission on Judicial Action to help pay the legal fees of the Ohio Psychiatric Association,

on a matching basis up to \$5,000, in its legal challenge to a state employee program that has contracted with a managed care company (Sept. 1990).

Liaison Activities

1. Authorized the President to appoint a psychiatrist administrator recommended by the American Hospital Association (AHA) to serve (at APA expense) as a consultant to the Council on Psychiatric Services and invited an AHA staff member to attend (at AHA expense) meetings of the Council on Economic Affairs (both positions will have multiyear terms) (March 1991).

2. Requested that the AHA appoint an APA-recommended member to serve (at AHA expense) as a member on the AHA Governing Council of the Section for Psychiatric and Substance Abuse Services and requested that an APA staff member participate (at APA expense) in the deliberations of the AHA council (both positions will have multiyear terms) (March 1991).

3. Voted that APA and the AHA strongly consider the appointment of liaisons representing the interests of psychiatry and hospitals on key policy development committees or commissions critical to concerns of both organizations (March 1991).

4. Voted to resign from the Council of Medical Specialty Societies (Sept. 1990) and later voted to rejoin the organization, subject to further review of its progress throughout the year (Dec. 1990).

5. Endorsed APA's efforts to interact with the National Foundation for Brain Research, as long as the interaction reflects APA policy (March 1991).

6. Authorized APA's participation in the planning and implementation of a conference on interdisciplinary collaboration in the delivery of mental health care; authorized APA's participation with other members of the Joint Commission on Interprofessional Affairs in seeking funding to support the conference (following established procedures and working in conjunction with the Medical Director's Office); allocated \$5,000 from the 1991-1992 contingency fund as APA's matching contribution to the conference (Sept. 1990, Dec. 1990).

7. Ratified an Executive Action taken by the President, Speaker, and Medical Director to approve APA cosponsorship of the Behavioral Healthcare Symposium to be held Sept. 5-7, 1991, in Boston (March 1991).

8. Authorized the Committee on State and Community Psychiatry Systems to establish liaison with the National Association of State Mental Health Program Directors and the National Council of Community Mental Health Centers and to explore developing reciprocal relationships with these groups, at no additional cost to APA (Dec. 1990).

9. Authorized the President to appoint an APA member to the Utilization Review Accreditation Committee's board of directors (March 1991).

10. Approved APA's becoming an organizational member of the Society for the Advancement of Women's Health Research, with representation on its executive committee (June 1990).

11. Ratified the Executive Action taken by the President, Speaker, and Acting Medical Director, Dr. Carolyn B. Robinowitz, to authorize contributing \$100 to the Federation of Organizations of Professional Women for a reception for female recipients of federal fellowships held on March 15, 1991 (March 1991).

Managed Care

1. Reported out of executive session that APA should increase education of members about the economics of practice in general and managed care in particular; encouraged increasing publicity about the 800 managed care telephone line; decided to request members to submit patient case material describing problems with the managed care system to develop a data base on specifics; directed staff to ask the district branches to help solicit this information; discussed the possibility of including the contents of the *Eco-Facts* newsletter in *Psychiatric News* (June 1990).

2. Approved the recommendation of the Editorial Review Panel that "Psychiatry and Managed Care Systems: Toward the 1990's" not be published but be made available on request through the Office of Psychiatric Services (March 1991).

3. Requested that legal counsel, in consultation with the Ad Hoc

Committee on Managed Care Issues, continue exploring the feasibility of national litigation designed to reverse the intrusive and abusive activities of the managed care industry; in particular, requested that the Board be presented with specific litigation proposals for consideration and analysis at its December 1990 meeting; authorized up to \$30,000 for legal fees related to this work; acknowledged the importance, complexity, and ultimate financial dimensions of a litigation strategy and stated that these considerations could be best analyzed in the context of a concrete litigation proposal (Sept. 1990).

4. In executive session, voted to endorse a legal action, subject to Assembly approval of such litigation and guidance regarding necessary funding, against proper parties in the managed care industry to prevent inappropriate, harmful, and unlawful intrusions into the provision of psychiatric service to mentally ill patients (Dec. 1990).

5. Allocated up to \$30,000 from the Board's 1991 contingency fund for further work on preparation of such litigation, with the understanding that the monies would be repaid to the contingency fund from any monies subsequently raised to support this litigation (Dec. 1990).

6. In executive session, voted to clarify its December 1990 action regarding possible legal action against parties in the managed care industry, stating that it is seeking input from the membership through the district branches and the Assembly about whether APA should pursue such legal action to prevent inappropriate, harmful, and unlawful intrusions into the provision of psychiatric services to mentally ill patients; further, voted to state that the Board seeks input from the membership regarding funding for this potential legal action (March 1991).

7. Authorized the Committee on Managed Care and the Committee on Ethics to seek approximately \$27,250 in outside funding, following established procedures and working in conjunction with the Medical Director's Office, to support a conference on managed care and ethics (March 1991).

Membership

1. Approved advancement of 185 General Members to Fellow status, approved advancement of two Life Members to Life Fellow status, and deferred advancement of 61 General Members to Fellow status (names on file) (Dec. 1990).

2. Authorized dropping one Member-at-Large, reinstating another Member-at-Large, advancing an Associate Member-at-Large to a General Member-at-Large, and approving one application for Member-at-Large (names on file) (Sept. 1990).

3. Approved a proposal from Meridian One Corporation to offer discounts to members for office equipment, Sprint long-distance telephone service, and an Alamo car rental program (June 1990).

4. Approved 25 applications for Corresponding Membership, approved five nominations for new Corresponding Fellows, and approved two nominations and deferred four nominations for advancement from Corresponding Membership to Corresponding Fellowship (names on file) (Dec. 1990, March 1991).

5. Approved dues relief and/or transfer to Inactive status for 140 members, denied dues relief and/or transfer to Inactive status for 26 members, and approved 67 requests for dues relief and/or transfer to Inactive status, pending district branch recommendations (June 1990, Sept. 1990, Dec. 1990).

6. Expelled Dr. Joanna M. Gaworowski from APA and the North Carolina Psychiatric Association for violation of section 1, annotation 1, and section 2, annotation 1, of the "Principles of Medical Ethics With Annotations Especially Applicable to Psychiatry" (June 1990).

7. Expelled Dr. Alvis J. Scull from APA and the Southern California Psychiatric Society for violation of sections 1, 2, 3, and 4 of the "Principles of Medical Ethics With Annotations Especially Applicable to Psychiatry" (June 1990).

8. Expelled Dr. David Logan from APA and the Hawaii Psychiatric Society (Dec. 1990).

9. Approved the nomination of Norman Sartorius, M.D., for Distinguished Fellowship and approved the nominations of Ellen Frank, Ph.D., and Myrna Weissman, Ph.D., for Honorary Fellowship (Dec. 1990).

10. Denied two requests for exemption from the APA/district branch dual membership requirement submitted by the Florida Psychiatric Society and the San Diego Society of Psychiatric Physicians (names on file) (Dec. 1990).

11. Dropped from APA and district branch membership one member of the Bronx District Branch for failure to advance from Member-in-Training status (name on file) (Dec. 1990).

12. Denied a request from a Medical Student Member of the Massachusetts Psychiatric Society for permission to remain a member of APA until July 1991, when the member expected to be enrolled in a psychiatric residency (the member is no longer in medical school) (name on file) (Dec. 1990).

13. Denied three applications for Associate Membership submitted by the Northern California Psychiatric Society, the Quebec and Eastern Canada District Branch, and the Western New York Psychiatric Society (names on file) (Dec. 1990).

14. Denied two applications for General Membership submitted by the Quebec and Eastern Canada District Branch and the Oklahoma Psychiatric Society (names on file) (Dec. 1990).

15. Authorized the necessary resources for the Office of Membership, working in concert with the district branches, to develop and implement a plan to recruit psychiatrists who are not now members of APA and to reduce attrition among current members (June 1990).

16. Authorized dropping from APA membership as of Oct. 1, 1990, one member who was in arrears for 1988 APA dues (name on file) (Sept. 1990).

17. Dropped from APA membership 538 members whose dues were in arrears for 1989 and authorized administrative reinstatement for those who returned to good standing by Jan. 31, 1991, and who were also in good standing in their district branches (names on file) (Dec. 1990, March 1991).

18. Authorized dropping from APA membership 251 members who had resigned from or were dropped by their district branches and authorized administrative reinstatement of those who returned to good standing in their district branches and who were also in good standing in APA (June 1990, Sept. 1990, Dec. 1990, March 1991).

19. Authorized dropping from APA membership as of Oct. 1, 1990, five members who had failed to join district branches (names on file) (Sept. 1990).

20. Terminated APA and district branch membership for Dr. Robert A. Komer, whose license was revoked by the Michigan Department of Licensing and Regulation because of conduct that would be unethical under the "Principles of Medical Ethics With Annotations Especially Applicable to Psychiatry" and reported this action to the National Practitioner Data Bank (Dec. 1990).

21. Terminated APA and district branch membership of Dr. Barry Moore, whom the North Carolina Psychiatric Society had expelled because of a number of violations of the "Principles of Medical Ethics With Annotations Especially Applicable to Psychiatry" and reported this action to the National Practitioner Data Bank (Dec. 1990).

Menninger, Karl

1. Voted to convey to Dr. Karl Menninger the love, respect, and good wishes of the Board of Trustees and the past Presidents of the Association (June 1990).

Minority Issues

1. Approved the "Position Statement on Homosexuality and the Armed Services" (Dec. 1990).

2. Approved the "Position Statement on Homosexuality and the Immigration and Naturalization Service" (March 1991).

3. Authorized the Committee of Hispanic Psychiatrists to seek \$50,000 in outside funding, following established procedures and working in conjunction with the Medical Director's Office, to develop a data base on individuals and organizations involved in Hispanic mental health services, including psychiatrists, special psychiatric societies, and national organizations (Dec. 1990).

4. Approved the recommendation of the Editorial Review Panel that the manuscript submitted by the Committee on International Medical Graduates be made available on request rather than formally published (March 1991).

5. Agreed to lend APA moral support for the establishment of a national clearinghouse that will collect, verify, and maintain documents and credentialing information for all graduates of international medical schools (Dec. 1990).

6. Approved the following APA policy: a) APA advocates reasonable uniform licensing standards (education, examination, and experience) and b) APA opposes discrimination against international medical graduates; further, requested the Joint Commission on Government Relations to monitor the progress of efforts to develop uniform licensing and a clearinghouse of international medical graduate records, requesting the commission to report to the Assembly about these matters periodically (Dec. 1990).

7. Authorized the APA President and/or Medical Director to communicate with Dr. Frederick Goodwin, ADAMHA administrator, regarding APA's concerns about the "Guidelines for Supplements for Underrepresented Minorities in Biomedical and Behavioral Research by ADAMHA" (Dec. 1990).

National Issues

1. Accepted the "Guidelines on the Role of the Psychiatrist When Requested to Provide Information About Patients for Security Clearance" (Dec. 1990).

2. Declined to endorse Area IV Action Paper 2, "The Importance of Preserving Existing Treatment Relationships When an Exclusive-Provider or Other Restrictive Mental-Health System Is Imposed on a Patient in Treatment," which was then referred to the Joint Reference Committee and the Committee on Managed Care for their consideration; stated that the Board supported the sense of the paper because of the importance of continuity of patient-physician relationships in treatment (Dec. 1990).

3. Approved the report of the Task Force on Psychiatric Services to Mentally Retarded Adults for publication, either in the "Official Actions" section of the *American Journal of Psychiatry* or as part of the APA task force report series (Dec. 1990).

4. Approved the position statement "Use of Stigma as a Political Tactic" (June 1990).

5. Reaffirmed APA's commitment to ending discrimination against mental illness; voted to encourage district branches to pursue whichever methods best meet their regional needs in addressing this common goal; voted to convey to the district branches a sense of urgency in reviewing possible options in addressing the need for proper treatment of mental illness whenever possible (June 1990).

6. Established the five-member Committee on Universal Access to Health Care within the Council on Economic Affairs, which will have close linkage to the Joint Commission on Government Relations for the implementation of any policy decisions by the Board on this subject, with the understanding that funding for the committee in the 1991 APA budget would be requested and that the committee's work would not begin until funding was available; voted to send the report of the informal work group on universal health care to the new component (June 1990).

Pharmaceutical Industry

1. Voted to cosponsor with Burroughs Wellcome a theater production using depression as a theme, which would premier in late winter 1991 in New York City and be performed again at the 1991 APA annual meeting (June 1990).

2. Authorized APA to collaborate with Burroughs Wellcome to develop a balanced scientific educational program on depression, subject to APA policy and guidelines in working with industry (March 1991).

3. Authorized the Joint Commission on Government Relations and other appropriate components (e.g., AMA Section Council on Psychiatry) to develop and pursue a strategy that would reduce the costs of clozapine treatment and remove the regulations that impede physicians' management, evaluation, and treatment of their patients taking clozapine; further, requested that appropriate components (e.g., the Committee on Confidentiality) establish confidentiality guidelines for the nationwide listing of patients used in the current case management system for clozapine (June 1990).

4. Ratified the Executive Action taken by the President, Speaker, and Medical Director to approve a statement on clozapine recommended by the Committee on the Chronically Mentally Ill and the Council on Psychiatric Services; further, authorized APA to act through all possible channels to ensure that all patients who would benefit from this medication have access to it (June 1990).

Practice Guidelines

1. Approved a number of steps to be taken in the development of practice guidelines by APA, including establishment of criteria for development of guidelines, active involvement of practicing clinicians in the process, and identification of procedures for selection, review, and approval of these guidelines (June 1990).
2. Established the Steering Committee on Practice Guidelines; approved discharging the Work Group on Practice Parameters; encouraged the steering committee to review existing practice guidelines and make recommendations to the Board (Sept. 1990).
3. Voted to substitute the term "practice guidelines" for "practice parameters" (Sept. 1990).

Psychiatric News

1. Reappointed Dr. Mary Jane England to a 4-year term on the *Psychiatric News* Editorial Advisory Board (she had been serving the remainder of the late Dr. William Sorum's term) (March 1991).
2. Appointed Ms. Mary Nowesnick as a lay journalist member of the Editorial Advisory Board, replacing Ms. Barbara Culliton, who had resigned (March 1991).
3. Granted permission to *Psychiatric News* to add an editorial section to *Psychiatric News*, with the understanding that this section may be controversial and may elicit negative comments from members (Dec. 1990).

Public Mental Health

1. Authorized the Council on Psychiatric Services and a consortium of public psychiatry components to implement a May 1990 Assembly action paper that requested APA to develop a clearinghouse to coordinate, promulgate, and promote optimal systems of mental health care delivery (Dec. 1990).
2. Endorsed the "Guidelines for the Chief Executive Officer and the Medical Clinical Director in Public Mental Health Facilities," with the understanding that the document will be made widely available to public mental health facilities (June 1990).
3. Agreed that a psychiatrist from the U.S. Public Health Service would routinely be appointed as a consultant to the Committee on Psychiatric Services in the Military, if possible, at no additional cost to APA (Dec. 1990).

Quality Assurance

1. Agreed that APA should vigorously oppose the proposed CHAMPUS reductions in authorized hospitalization days and residential treatment days and referred this matter to the Joint Commission on Government Relations for additional consideration and action (Dec. 1990).
2. Approved the "Manual of Quality Assurance," with the understanding that the disclaimer given in the report would be used (March 1991).

Research

1. Authorized an expenditure of up to \$10,000 for contributions to the Coalition for Brain Research and to the Medical Sciences Legal Defense Fund, the exact appropriation for each to be determined in consultation with Dr. Herbert Pardes, chairperson of the Council on Research (the Council on Research provided \$5,000 from its 1990 budget and the Joint Reference Committee allocated the balance from its 1990 contingency fund) (Dec. 1990).
2. Requested the Committee on Biographical Directory and Research on Psychiatric Professional Activities to develop a plan to implement the recommendations in the report of the Work Group on Data Bases for Psychiatry and to report this plan to the Board (March 1991).
3. Endorsed the intent of Area I Action Paper 1 (i.e., for APA to consider incorporating culture-specific disorders in DSM-IV) and referred this paper to the Task Force on DSM-IV (Dec. 1990).
4. Approved publishing the report of the Task Force on Prevention Research in the *American Journal of Psychiatry* (June 1990).
5. Approved the report of the Task Force on Quantitative Electro-

physiological Assessment for publication in the "Official Actions" section of the *American Journal of Psychiatry* (Dec. 1990).

6. Approved the report of the Task Force on Tardive Dyskinesia for publication as an APA task force report, with the understanding that it would be reviewed by legal counsel and that Dr. Hartmann would approve any changes in wording (Dec. 1990).

Resource Development

1. Authorized the establishment of the APA pooled income fund, as recommended by the Resource Development Committee (June 1990).
2. Created the APA Corporate Partners Program (Sept. 1990).
3. Authorized the Resource Development Committee to proceed with the establishment of a supporting 501(c)3 foundation (Sept. 1990).
4. Approved the formation of the American Psychiatric Foundation, Inc., as a nonprofit corporation in the District of Columbia and voted to instruct the Association's legal counsel to file the articles of incorporation of American Psychiatric Foundation, Inc., as presented to the Board in the report from the Resource Development Committee (Dec. 1990).
5. Approved the appointment of the following individuals as interim directors of the American Psychiatric Foundation, Inc.: Drs. Elissa Benedek, Mary Jane England, Robert Garber, Edward Hanin, Lawrence Hartmann, Thomas Pfahler, Melvin Sabshin, and Howard Wallach (March 1991).

Sesquicentennial

1. Authorized the Ad Hoc Committee to Plan for APA's Sesquicentennial to begin contacting the pharmaceutical companies and allied groups who meet during the annual meeting to ascertain their plans for the 1994 annual meeting and inform them that the use of the logo created for the sesquicentennial or the distribution of any materials that commemorate the sesquicentennial must be approved by the ad hoc committee or its designee (March 1991).
2. Authorized the ad hoc committee to seek outside funding for projects associated with the sesquicentennial, following established procedures and working in conjunction with the Medical Director's Office (March 1991).
3. Authorized the ad hoc committee to petition the U.S. Postal Service for a stamp honoring Benjamin Rush, M.D., to be released in 1994 (June 1990).

Subspecialization

1. Endorsed the establishment of added qualifications in addictive disorders in psychiatry contingent on the approval of the Commission on Subspecialization and the Assembly (approved by the Commission on Subspecialization in October 1990 and the Assembly in November 1990) (June 1990).
2. Approved the definition, criteria, and procedures that are to be used by APA in determining whether or not an applicant group is qualified to become a subspecialty (June 1990).
3. Authorized a letter over the signature of APA leaders to the ABPN expressing APA's view that special qualifications in EEG should be made available to eligible psychiatrists, as well as to neurologists (June 1990).

Youth

1. Approved the "Position Statement on Child Abuse and Neglect" (March 1991).
2. Endorsed APA's cosponsorship of the 1991 National Conference to Abolish Corporal Punishment in the Schools, at no cost to APA (March 1991).
3. Approved the report of the Task Force on Juvenile Justice Issues for publication in the "Official Actions" section of the *American Journal of Psychiatry* (June 1990).
4. Approved for publication the *Handbook on Psychiatric Practice in Juvenile Court* and congratulated the eight-member Committee on Juvenile Justice Issues, especially Dr. Michael Kalogerakis, who was chairperson during preparation of the handbook, for its remarkable work and product (March 1991).

5. Endorsed the term "emotional and behavioral disorders" to replace "serious emotional disturbances" (June 1990).

6. Approved the "Position Statement on Drugs of Abuse in School-Aged Children" (June 1990).

7. Authorized implementation of the Assembly's recommendation that APA communicate its willingness to work with the American Academy of Child and Adolescent Psychiatry and other appropriate organizations to promulgate model criteria for the admission of adolescents to psychiatric facilities (June 1990).

8. Established the 3-year, five-member Task Force to Study the Use and Abuse of Psychiatric Hospitalization of Minors within the Council on Children, Adolescents, and Their Families (Dec. 1990).

9. Authorized the Council on Children, Adolescents, and Their Families to seek \$30,000 in outside funding, following established procedures and working in conjunction with the Medical Director's Office, to support the Task Force to Study the Use and Abuse of Psychiatric Hospitalization of Minors (Dec. 1990).

10. Authorized cosponsoring with the American Association for the Advancement of Science, at no expense to APA, a conference on

physical and mental disabilities that children experience as a result of traumatic human rights violations (Dec. 1990).

11. Approved the "Position Statement on the Federal Role in Children's Mental Health" (March 1991).

12. Endorsed the Institute of Medicine's report "Research on Children and Adolescents With Mental, Behavioral and Developmental Disorders: Mobilizing a National Initiative" and endorsed the activities recommended in the report and the recommendations by the Council on Children, Adolescents, and Their Families and the Joint Reference Committee (June 1990).

13. Ratified an Executive Action taken by the President, Speaker, and Medical Director authorizing the Committee on Psychiatry and Mental Health in the Schools to seek outside funding, following established procedures and working in conjunction with the Medical Director's Office, for preparation of guidelines for psychiatrists who provide consultative and clinical services to schools (Dec. 1990).

14. Endorsed the "Position Statement on School-Based Health Clinics" (Dec. 1990).

Report of the Treasurer

Mary Jane England, M.D.

EXECUTIVE SUMMARY

Economic environment of the United States

- Economy is in recession.
- Unemployment is rising.
- Financial institutions are in crisis.

Growth in membership

- Membership rose from 25,814 in 1980 to 36,918 in 1990.
- Greatest increase (an increase from 1,365 to 5,760 members, or 322%) was in the Members-in-Training category.

Growth in operating budget

- Operating budget grew from \$8.7 million in 1980 to almost \$24 million in 1990.
- Operating budget grew less than 2% in 1991.

Growth in member dues

- Compounded growth in dues from 1980 to 1990 was over 100%.
- During the 1980s, dues inflated by about 8% per year on average, in contrast to an increase in the cost of living of about 4.2% during the same period.
- Dues increase was same as the projected increase in the cost of living for 1991, 4.65%.
- In 1991, dues were increased by \$20, which was half of the 1990 increase of \$40.

Term debt—Has been eliminated.

Line of credit borrowing—Projected to increase to \$5 million in 1991.

Publications and advertising sales—Were strong in 1990 and early 1991.

Net worth—Stands at \$10.3 million.

Financial forecasting—Has been enhanced.

Multiyear financial planning—Implementation approved by Board of Trustees.

GENERAL

This report is prepared from audited figures for the fiscal year that ended Dec. 31, 1990. The data presented also appear in the auditor's annual report.

Table 1 is a statement of our financial condition, taken from the independent auditor's report, and table 2 reflects functional revenues and costs. These will provide the membership with the information needed to assess the operation and financial condition of the Association.

SUMMARY OF FISCAL RESULTS OF 1990 OPERATIONS

During 1990, APA's general fund programs continued their strong programmatic and fiscal performance. General fund operations in 1990 resulted in income of \$24,907,182, contrasted with expenses of \$24,257,444, for a surplus from operations of \$649,733. During 1990, APA sold its interest in Professional Risk Management Services, Inc., and the proceeds helped balance the 1990 budget and make possible the surplus from 1990 operations.

SERVICES FOR MEMBERS

APA's most important function is service to its members. In the last decade, our membership has grown from 25,814 at the end of 1980 to 36,918 in December of 1990, for an increase of 11,104 members, or 43.0%, which represents an average net gain of over 1,000 members per year. However, a number of general trends have been identified that suggest slower growth of dues income in the future, primarily a stabilization of the number of new members and a rapid increase in the number of dues-exempt members. As shown in table 3, the rate of membership growth is not equally distributed among the various categories of membership; it is higher for dues-exempt members than for dues-paying members.

The enrollment and continuing membership of medical students (since 1984) and residents have important implications for the future growth and strength of the Association. Several measures have been taken to promote growth in these categories, including an amendment on this year's ballot to set a one-time fee for medical students (as opposed to annual dues) and to exempt them from having to belong to a district branch until they graduate from medical school. With

TABLE 1. APA Balance Sheets as of Dec. 31, 1990 and 1989

Item	Amount (dollars)	
	1990	1989
Assets		
Current assets		
Cash and cash equivalents	1,451,734	1,325,966
Marketable securities	652,561	651,416
Accounts receivable, less allowance for doubtful accounts	1,387,536	1,234,876
Grants and contracts, approved and in process	2,172,286	1,482,399
Notes receivable	0	94,500
Advances to affiliates	1,128,239	799,461
Publications inventory	495,093	523,027
Prepaid expenses and other current assets	396,004	362,063
Total current assets	7,683,453	6,473,708
Property and equipment		
Land	5,187,470	5,187,470
Building—leasehold interest and improvements	7,104,926	6,986,914
Furniture and equipment	2,446,675	2,393,309
Subtotal	14,739,071	14,567,693
Less accumulated depreciation and amortization	2,804,993	2,367,819
Total property and equipment	11,934,078	12,199,874
Other assets		
Notes receivable, less current maturities	0	130,500
Deferred expenses, net of accumulated amortization	2,615,926	2,218,591
Deferred land rent	809,578	765,004
Nonmarketable securities	0	75,000
Intangible pension asset	231,307	224,324
Total other assets	3,656,811	3,413,419
Total assets	23,274,342	22,087,001
Liabilities and fund balances		
Current liabilities		
Current maturities of long-term debt	0	225,000
Accounts payable	1,381,929	2,174,850
Accrued expenses	1,865,145	1,824,206
Deferred revenue	1,344,300	1,192,574
Deferred amounts		
Restricted—grants and contracts	1,508,808	705,640
Restricted—awards and special projects	2,165,160	1,600,527
Total current liabilities	8,265,342	7,722,797
Other liabilities		
Capital lease obligation, less current maturities	4,430,070	4,442,544
Accrued pension cost	231,307	224,324
Total other liabilities	4,661,377	4,666,868
Fund balances		
Unappropriated	6,078,042	5,428,304
Appropriated	150,000	150,000
Building	4,119,581	4,119,032
Total fund balances	10,347,623	9,697,336
Total liabilities and fund balances	23,274,342	22,087,001

respect to Members-in-Training (residents), the most important source of new General Members, APA has changed its present three-step phase-in dues structure to a revenue-neutral seven-step scale that will ease the financial burden of members advancing to General Member status after completion of residency.

The rapid growth of dues-exempt members had made the need for services disproportionately large in relation to the generation of dues revenue. To minimize this imbalance, the 1992 ballot will in-

TABLE 2. APA's Functional Revenues and Costs for Fiscal Years 1990 and 1989

Item	1990	1989
Functional revenues		
Percent from each function		
Publications		
Advertising	18.84	15.97
Subscriptions and related fees	6.72	5.65
Book sales	16.65	17.50
Member services		
Dues from members	36.40	34.58
Meetings income	12.78	12.05
Other income related to member services	2.37	2.31
Other income (investments, overhead on grants, contributions, etc.)	6.24	11.94
Total revenues (dollars)	24,907,182	24,726,542
Functional costs		
Percent for each function		
Governance and member component activities (Board of Trustees, Assembly, joint commissions, councils, and components)	15.50	14.52
Publications (APA journals and book sales)	29.76	28.99
Public affairs (public information and government relations)	10.33	10.10
Member services (membership services and educational programs)	27.16	24.44
General administrative costs	17.25	13.48
Cost of abandoned project	0.00	8.47
Total costs (dollars)	24,257,444	26,140,609

clude amendments to permit charging new Life Members dues for the first 10 years after conversion to Life status, whereas Life Members have paid no dues in the past. In addition, beginning in July of 1991, all Life Members/Fellows will pay an annual communications fee for continued receipt of the *American Journal of Psychiatry*, although *Psychiatric News* will remain free to Life Members/Fellows.

Membership recruitment projects have been expanded to include special mailings to female psychiatrists, greater collaboration with other organizations, such as the American Medical Association, forgiveness of over 1 year's dues for former members wishing to reinstate, and continued revision of membership policies and procedures to facilitate enrollment.

All of these measures, including changes to the dues structure, reflect APA's goals of increased membership growth and retention despite a plateauing of the pool of potential members. At the same time, they represent sound membership and fiscal policies and are compatible with APA's overall strategic planning efforts.

Our large membership of almost 37,000, a strong financial base, and the increasingly complex problems and opportunities facing our profession have led to the development and provision of expanded services for APA members. This growth in services has been primarily in government relations, public affairs, education, Office of Membership activities, economic affairs, and research.

DEBT MANAGEMENT

Another important message in this Treasurer's report relates to borrowing. First, APA's borrowing has increased over the past few

TABLE 3. Change in Dues-Paying and Dues-Exempt APA Membership Between 1980 and 1990

Membership Category	Number of Members		Percent Change
	December 1980	December 1990	
Dues-paying members	22,008	29,263	+32.97
Members-in-Training	1,365	5,760	+321.98
General Members	16,137	19,791	+22.64
Associate Members	470	192	-59.15
Fellows	4,036	3,520	-12.78
Dues-exempt members	3,806	6,887	+80.95
Life Members/Fellows	2,643	5,285	+99.96
Inactive Members/Fellows	684	886	+29.53
Other (Honorary, Distinguished, Corresponding Members)	479	716	+49.48
Medical Student Members	0	768	

years to an estimated \$5 million in 1991 and \$6.5 million in 1992. Second, APA's need to borrow is increasing as the position of the banking community throughout the nation is deteriorating. Banks, in general, are experiencing lower profits or deficits, nonperforming loans, more strict liquidity standards from federal regulators, and less confidence on the part of consumers. As a result, banks are becoming less willing and able to make loans, and when loans are obtained, they are often for smaller amounts with less favorable contractual terms. Third, APA's fiscal stability can be enhanced by reversing the current trend toward more borrowing. This, in turn, can be realized by increasing liquid reserves through yearly surpluses from operations earmarked specifically for this purpose.

We are formalizing our strategic financial planning efforts in order to 1) identify opportunities to increase efficiency through reorganization and technology, 2) control growth in expenses, 3) increase revenue from nondues sources, and 4) increase prioritization in providing programs for our members and our patients.

Also, we are strengthening the budget process and financial forecasting. These courses of action can help APA move to a new and more meaningful position with respect to debt reduction. During the past decade the Association has viewed debt reduction from a somewhat defensive and reactive perspective—as paying off loans on time. We can now move to a higher plane in regard to debt reduction—to a more aggressive and more proactive stance—by not borrowing (or at least borrowing less) in the first place. We can move from a position of leverage to a position of cash. We can move from merely honoring commitments to banks to honoring a commitment to help APA achieve self-sufficiency.

The Board of Trustees took an important step in this direction during its March 1991 meeting when it approved expanding the functions of the Budget Committee to include short-term (3- to 5-year) financial planning with a major goal of building liquid reserves. It is envisioned that the Budget Committee will meet twice during 1991 and will be an integral part of APA's policy apparatus in the years ahead.

Even though a primary APA goal should be the minimization of borrowing, it is also important that the Association devote thoughtful consideration and oversight to its current loans. During 1990, APA negotiated an excellent loan package with American Security Bank, N.A. Highlights of the loan package as it is currently configured are as follows:

Term loan—maximum limit of \$1,500,000 at 1/2% over the prime rate. As of Dec. 31, 1990, there were no borrowings through this mechanism. Any future borrowings are due and payable by Oct. 1, 1993.

Line of credit—maximum limit of \$5,000,000 at 1/2% over the prime rate. The stability of the cash budget was evidenced by the fact that the line of credit was used during only 4 months of 1990 and only \$2,750,000 needed to be used.

The Association has consistently met its obligations for all loans—fully and on time—past and present.

NET WORTH

The Association's stated net worth (reserves) has increased from approximately \$4 million in the mid-1970s to over \$10.3 million today (\$10,347,623). This stated figure is extremely conservative, since it does not include the estimated increase in the value of the 1400 K Street property, which APA purchased in 1980. If this estimated increase in land value were to be included as part of APA's stated net worth, the figure would stand at about 4 1/2 times our net worth in the mid-1970s. Even if inflation is taken into account, the increase in the Association's net worth in recent years is particularly impressive, from \$7,486,501 in 1984 to \$10,347,623 in 1990. As already noted, the Association is planning not only for a continued growth of its net worth, but for an enhancement of liquid (cash) net worth.

BUSINESS CYCLE

Like many other organizations, APA operates within a business cycle that heavily influences its cash flow, the level of reserves, and other aspects of its fiscal status. The cycle comprises a series of fiscally strong years followed by weak years—then the cycle continues. Fiscal years 1985 through 1988 were strong years. We have moved into a downturn that is projected to continue through 1993, and it is expected that there will be some relief in 1994 and that 1995 will be the next fiscal year showing signs of significant additional financial strength.

It is important to note that the downturn in APA's business cycle occurred in conjunction with recessionary pressures, problems in the banking community, and a leveling off of dues revenues.

INVESTMENTS

The Investment Advisory Committee has guided the Association's investment program over the last 15 years. The stated investment policy of the Association is "to employ sound investment vehicles affording maximum return consonant with safety of capital, i.e., the type of investment a prudent individual would seek." With this in mind, safety of capital has been identified as the first objective of the investment program. In 1980, the Association carefully reviewed its investment alternatives and shifted a majority of its investment resources from ownership of securities to an ownership position in the new headquarters building project. The investment portfolio, as distinguished from the investment in the APA office building, showed balances for years 1989 and 1990 of \$651,416 and \$652,561, respectively. There were no significant additions to the investment portfolio in 1990, since the interest and dividends were used for operations rather than being reinvested in the portfolio.

The current policy of the Association is to balance investments between debt instruments and common stocks, although more aggressive/defensive investment postures are taken from time to time in response to changes in market conditions. The market value portfolio valuation of Dec. 31, 1990, indicated the following approximate distribution of investments: 74% in debt instruments, 2% in cash, and 24% in stocks. The Association's investment portfolio is under continuing review and management.

PUBLICATIONS

The Association and its publishing affiliate, the American Psychiatric Press, Inc. (APPI), maintain approximately 250 book titles in inventory. Total income for the APA publication program amounted to \$7,203,373. Of this total, \$4,146,143 was provided by sales of APA publications and products, and \$3,057,230 was accounted for by sales of APPI books and products.

Psychiatric News generated income of \$3,750,373, offset with expenses of \$1,592,175, for a surplus of \$2,158,198. This amount is \$577,078 more than the budgeted surplus of \$1,581,120.

The *American Journal of Psychiatry* produced revenues of \$2,936,361 and incurred expenses of \$2,010,657, for a surplus of

\$925,704. This total is \$414,948 more than the budgeted surplus of \$510,756.

The journal *Hospital & Community Psychiatry* realized revenues amounting to \$1,150,551 and expenses of \$892,874, for a surplus of \$257,677. This amount is \$95,024 more than the budgeted surplus of \$162,653.

SUMMARY

The 1980s proved to be a period of expansion for APA—when income-producing programs achieved greater successes each year and when service programs grew in resources, expertise, and productivity. This growth was supported by our environment as well as by forces within the Association.

Some of the elements of the 1980s must be continued. We must continue the efforts of the past decade to continually refine our plan-

ning efforts, improve program management, and more effectively monitor expenditures.

On the other hand, many of our strategies of the 1980s must be revised for the 1990s to achieve compatibility with a new environment and with new needs and expectations of our members. We need to formalize strategic planning in order to increase cash reserves, which will reduce the need for bank loans and member dues increases. We need to streamline APA operations, maximize nondues income, and limit the growth of expenditures. The business cycle should be smoothed out so that surpluses from stronger years can help support operations in weaker years. Organizational growth should be checked by shifting our priorities from growth based on increasing resources to greater effectiveness and efficiency than are now present.

I appreciate the opportunity to serve as your Treasurer during this period of professional and fiscal challenge. I look forward to working with you toward meeting the high-priority needs of our Association, our profession, and our patients.

Report of the Medical Director

Melvin Sabshin, M.D.

During my 17-year tenure as APA Medical Director, the annual report has become a useful reflection of progress and problems. We have indeed been coping with extraordinary challenges; the themes of socioeconomic and political ferment have dominated my reports for some time. The coping process has been accompanied by a steady growth in our membership and an increased diversity and complexity of the functions assumed by the national leadership and the Central Office. Since last year's report, we have faced many difficult decisions and actions, and I am pleased with the mood, strength, stability, productivity, and responsiveness of the organization. Both the tone and content of our activities are positive overall and demonstrate strong effective working relationships between staff and members. Dr. Benedek's thoughtful, energetic, and effective leadership is reflected in the strength and enhancement of many departments' efforts.

APA staff has shown remarkable efficiency and productivity. While the quantity of work continues to increase, we have been able to maintain high quality, even in the face of increasing demands in many arenas. This year, the Association has focused on how to provide the most cost-effective support and leadership for the diverse needs of more than 37,000 members while avoiding possible fragmentation from increased interest in subspecialization and a variety of forms of practice. We have devoted much energy to considering the impact of managed care on APA members and their patients. Through extensive resources devoted to scientific activities, we have begun a process of developing practice guidelines and continue to develop a reliable and valid diagnostic nomenclature. Our strength in public policy deliberations and in the decrease of stigma associated with care for mental disorders has depended heavily on our scientific growth and credibility as a field. We also have carefully monitored the Association's business-related work and fiscal affairs, as well as the more traditional specialty society membership efforts. To that end, we have held frequent discussions with counterparts in other medical specialties and in the other mental health disciplines.

I am sad to report that we have sustained major losses in APA leadership this year. Dr. George Ginsberg, Area II Representative and President of the New York State Psychiatric Society, died suddenly in February. George was a remarkable person whose concern for the field and its future were pivotal in a number of Association activities. George's thoughtful leadership added much to the deliberations of the

Assembly and its Executive Committee. He was intelligent and knowledgeable but also practical, attuned to issues of process and implementation, and ever sensitive to the needs and feelings of others. An excellent representative to the Joint Commission on Interprofessional Affairs, he also was a highly valued liaison to (and recently appointed incoming chairperson of) the APA Council on Medical Education and Career Development. His assistance was especially significant in our efforts to recruit psychiatrists and to bring residents into Association leadership. His family is in the process of determining how they would like to memorialize him, and we will work with them to find a formal and concrete commemoration.

The Assembly sustained another loss with the sudden death of Dr. Jose Arana, who recently was elected Minority Representative. Dr. Arana was Medical Director of the Carter Center and on the faculty of the University of Maryland, where he was a valuable resource in clinical and administrative activities.

We also mourn the death of Mrs. Evelyn Stone, an APA Honorary Member and a very special contributor to the Joint Commission on Public Affairs and the American Psychiatric Press, Inc. (APPI). Her warmth, humor, ever-present energy, and devotion to the best in psychiatry contributed much to our success.

Last October, APA held a very successful joint meeting with the German Society of Psychiatry and Nervous Diseases. The scientific sessions and collegial interactions were first rate. We all were most affected by the changing political scene in Europe and by the emotional events surrounding the unification of Germany. Dr. Johannes Meyer Lindenberg and his colleagues expended considerable effort to make the meeting particularly memorable. I am saddened to report that Dr. Meyer Lindenberg died in February. We remember with gratitude his many contributions to the meeting and to world psychiatry and extend our condolences to his family.

Staff changes highlight the balance between stability and growth, gains and losses. Last year, I informed you of the retirement of our Librarian, Ms. Zing Jung. I am pleased to announce the appointment of Mr. William Baxter, Archivist, as her successor. The Library has become a modernized storehouse of information with computerized data bases and audiovisual learning materials, in addition to books and journals. The Kenworthy Learning Center is an excellent resource for members and staff alike. I look forward to working with Mr.

Baxter in his new capacity. As we approach our sesquicentennial, the integration of our history with advances and plans for the future will be increasingly important.

There has also been change in the leadership of the Office of Education. Dr. Philip Bashook left APA in June 1990. I appointed Ms. Rosalind Keitt, Assistant Director for Administration, as Interim Director. We have temporarily delayed filling the position because of fiscal constraints. Ms. Keitt has been an extraordinarily effective leader who has worked well with the APA Council on Medical Education and Career Development and related educational organizations. She, Dr. Jeanne Spurlock, and Dr. Carolyn Robinowitz are to be commended for their work in strengthening our educational productivity and performance. At the same time, members of the educational community have voiced their hope that we fill the position as soon as possible, noting the importance of the position to psychiatry.

Since my last report to you, there have been some transitions in the Division of Government Relations. Mr. Fred Fedeli, Assistant Director, who was a major resource in the appropriations process, joined the staff of the National Alliance for the Mentally Ill as Director of Government Affairs. His successor, Ms. Sharon Cohen, former Director of Health Policy for the Alliance for Aging Research, has been a valuable resource in appropriations and related areas. Ms. Ellen Smith, Assistant Director, who moved to New Jersey last summer, was replaced by Mr. Nick Meyers, who served as Health Legislative Assistant to Congressman Jim Moody. Nick has been a tremendous asset to the division and to the APA Council on Aging and its components. Ms. Karen Howard, also an Assistant Director, resigned to become a consultant to the Jefferson Group. Her successor, Ms. Kelleen Jackson, came to APA from the office of Congressman Porter Goss, where she worked on veterans' issues, health care, and education. The continued high quality and quantity of the work of the Division of Government Relations attests to the skill of the new staff.

Last summer, we accepted with regret the resignation of Ms. Melanie Shipley as Managing Editor of the *American Journal of Psychiatry*. During her relatively brief tenure here, she was an excellent contributor to the excellence of the *Journal*. Ms. Linda Loy, Interim Managing Editor, performed remarkably as the staff worked diligently and effectively to ensure the high-quality content and timeliness of the *Journal* during its transition period. We welcome our new Managing Editor, Ms. Sandra Patterson, who previously worked at Slack, Inc., a publisher of medical journals and newspapers.

The collaboration of Dr. John Nemiah, the *Journal's* Editor, Dr. Nancy Andreasen, Deputy Editor, and staff continues the high standards of scientific excellence set by their predecessors. We continue to be impressed with the quality and quantity of articles in the *American Journal of Psychiatry*. The review articles particularly provide an excellent educational presentation of current scientific data. The *Journal* has, through increased use of technological support, improved the review process and shortened the time between submission and publication, and it is using desktop computer technology to decrease printing costs and increase efficiency.

We also note a transition at APPI, with the resignation of Mr. Tim Clancy, the first Editorial Director, and the appointment of Ms. Claire Reinberg to that position. She has worked closely with Mr. Ronald McMillen, General Manager, and Dr. Carol Nadelson, Editor-in-Chief, to ensure a painless and productive changeover.

There continues to be considerable interest in the APA governance process. The increased activities of the Assembly Executive Committee and its evolution as a major force in the governance of the Association were reflected at its interim meeting in September 1990, during the third, highly successful joint meeting with the Joint Reference Committee in March 1991, and in its expanding role in helping the Assembly plan and implement actions.

The Joint Reference Committee, too, has strengthened the input of its voting members while maintaining the importance of the participation of council chairpersons and emphasizing its role as "joint," representing both the Assembly and the Board. The Joint Reference Committee increasingly acts not simply as a referring body, but also as initiator and developer of proposals and directions. Drs. Elissa Benedek, Lawrence Hartmann, Edward Hanin, Thomas Pfahler, and Ronald Shellow are to be congratulated for their thoughtful yet pragmatic approach to both issues and processes. Ms. Corky Hart, Associate Director of the Office of Psychiatric Services, has been a marvel-

ous resource here, and the outstanding involvement and coordination of Ms. Jeanne Robb and staff in the Office to Coordinate the Board and Assembly make the process work smoothly.

Discussions about the roles of officers and trustees point to the increased involvement and interest of Board members, the expanded amount of business on the agenda of each meeting, and the need to set time aside for reflection and strategic planning for the Association. This interest is reflected in the ongoing discussion of subspecialization and liaison activities by the Assembly and Board Commission on Subspecialization. The American Board of Psychiatry and Neurology has responded positively to our recommendation to initiate the process for offering a certificate of added qualification in addiction psychiatry, and the first examination for added qualification in geriatric psychiatry took place this spring. We remain cognizant of the potential fragmentation and divisiveness of such efforts and the need to maintain organizational strength while maximizing input from all concerned.

This year, we have focused extensively on budget and financing. Over the past decade, we increasingly used outside funds (nondues income) to support new and high-priority projects. The termination of our Quality Assurance Program last year brought with it not only the costs of termination, but a loss of outside income. This resulted in the lack of funds for new projects but also brings the realization that increased funding is needed just to compensate for the inflationary growth in the costs of ongoing programs. In response to members' concerns, dues for 1991, which represent approximately 40% of the operating budget, have been held to an increase paralleling the increase in the rate of inflation. The recession and the conflict in the Middle East will affect both income (e.g., from advertising sales) and the costs of doing business (e.g., travel, postage).

We have begun improving cost-effectiveness through integration and consolidation of efforts, cutting or freezing vacant positions, and carefully reviewing priorities. As an example, we canceled the Public Affairs Institute scheduled for 1991. We monitor departmental expenditures closely. Staff and members alike will be feeling some pinch as we attempt to further streamline operations, and I recognize that the leadership will continue to be approached by many members requesting support for programs and activities they consider of the highest priority. The next few years will be a time of fiscal prudence, and our actions will be vital to the long-term health and function of the Association.

We have been actively assessing the impact of managed care and developing approaches to it. This task has been an interdepartmental staff effort coordinated by Dr. Robinowitz and involving staff in the Office of Psychiatric Services, Division of Government Relations, Office of Economic Affairs, and Division of Public Affairs, who are working with the Ad Hoc Committee on Managed Care Issues, which is chaired by Dr. Steven S. Sharfstein. While problems with managed care represent a major cause of member irritation and concern, APA members who work in or lead managed care organizations or settings feel that APA has been insufficiently aware of their interests, inasmuch as they too work to promote quality and cost-effective care. Responses to our Medicare/managed care 800 hot line have enabled us to collect, follow up on, and analyze data and information about members' experience with managed care and its impact on patient outcome and to identify problem organizations and approaches. In addition to considering the possibility of litigation to protect patient interests, we have developed model legislation for standards of managed care that will be an important resource for individual states. We have met with psychiatrists who hold leadership positions in the managed care industry and have shared members' concerns about practices that interfere with appropriate care. Staff is completing work on the "Managed Care Survival Manual," which will educate members about the process of managed care and utilization review.

There is substantial interest in practice parameters (standards and guidelines) within organized medicine. The Council of Medical Specialty Societies sponsored conferences on standards development, and the American Medical Association (AMA) has undertaken a major initiative for specialty societies to address the topic. Drs. Edward Hanin, John Hamilton, Harold Pincus, Carolyn Robinowitz, and Sara Charles represented APA in the initial efforts, and the Work Group on Practice Guidelines, chaired by Dr. John McIntyre, has initiated APA's activities leading to the promulgation of guidelines. We are exploring several sources of funding for this massive effort. I am op-

timistic and enthusiastic about working with other medical specialties on this important project and about the potential impact of such endeavors on the field.

A similar interdepartmental effort exists in our response to the release of clozapine. Dr. Hamilton has taken the lead in coordinating efforts to address such topics as access, cost, patient information, and protection. We have participated in several meetings with representatives of patient and consumer groups, state mental health commissioners, the Veterans Administration, researchers, and the pharmaceutical industry to consider how best to meet the needs of all concerned. A component of the APA Council on Research has developed draft recommendations on systems of monitoring and compliance that were shared with professional and consumer groups. There continue to be concerns about interference with the physician's role, as well as recognition of the need for appropriate care and patient safeguards.

Still another interdepartmental activity is related to the Persian Gulf war. Dr. Hamilton chaired the Staff Committee on Hostages, Military Personnel, and Their Families. This committee identified a roster of psychiatrists willing to provide services to hostages and their families, and it developed mailings to district branches on the provision of community services for families of military personnel, returning service personnel, and members of the general public who were anxious about the war. Through the Division of Public Affairs, APA distributed a pamphlet on coping with wartime stress, assisted in production of a 3-hour national call-in radio program on coping with wartime anxiety, and continues to work with the National Mental Health Association in its campaign "After the Yellow Ribbons Come Down" for returning military personnel and their families.

In each annual report, I have given special emphasis to our activities in government relations and public affairs. This year is no exception; indeed, I still rate these areas as the most important in producing genuine advances in diminishing stigma and increasing access to and reimbursement for care. Working in concert with our Joint Commission on Government Relations, Dr. John J. McGrath, chairperson, and commission members and network leaders, the Division of Government Relations continues to function as a sophisticated, effective force.

From my perspective, during this past year we have been much more visible and successful in our government relations activities than ever before. We have begun to develop clear and concrete objectives that have had an enormous impact on members and the patients they treat. We are most fortunate to have Mr. Jay Cutler leading our government relations efforts. He is widely respected on Capitol Hill and in the Administration, as well as by his colleagues. Our successes are a credit to his energy and knowledge and the long-range strategic planning and involvement of the field in Congressional communications.

Staff has worked with members of the Mental Health Liaison Group to develop a professional judgment budget for the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) and has begun a lobbying effort involving research scientists, clinicians, and patient advocates on its behalf. APA led the successful fight to secure funding increases for ADAMHA programs, which, despite the deficit reduction pressures, resulted in a 9.6% increase (\$2.9 billion) over fiscal year 1990. The research budget for the National Institute of Mental Health (NIMH) was \$458.7 million, representing an increase of 15% over 1990. These results point out the immense effectiveness of our educational efforts and the impact of the scientific advances in the field on Congress's willingness to fund more equitably.

The Congress seems poised to consider proposals to reform the provision of health care to the uninsured and underinsured. Current proposals range from reform of small-group health insurance coverage to implementation of a Canadian-style national health care single-payer system. Most of the bills introduced thus far include inpatient and outpatient treatment for mental disorders but with utilization limits not required of other illnesses. We will continue to monitor such efforts closely.

APA continued to work for an end to the discriminatory 50% co-payment for Medicare outpatient mental health treatment, but budget pressures prevented any action. We also were able to ensure that the Health Care Financing Administration adopted an explicit requirement that clinical psychologists caring for Medicare patients sign an

attestation of consultation with a physician as a condition of direct reimbursement for outpatient services.

APA has pressed both the Congress and the Department of Defense to oppose the proposal by Senator Daniel Inouye to establish a demonstration program within the Department of the Army to train clinical psychologists to prescribe drugs. Dr. Robinowitz, Mr. Cutler, and I were active on the Army Surgeon General's Blue Ribbon Panel addressing the topic, but the panel's recommendations were bypassed when the Army initiated a 1-year program to train two psychologists. The process for interaction continues, and we especially appreciate our members' input to Congress expressing concern about patient safety.

In anticipation of a renewed effort by psychologists to obtain prescribing privileges in Hawaii, Mr. Cutler, Ms. Katherine Becker, and I joined leaders of the Hawaii Psychiatric Medical Association to meet with key leaders of the Hawaii legislature to address these concerns. We also discussed the APA State/University Collaboration Project as a source of assistance to Hawaii's troubled state mental health system. While our contacts were successful, the issue was reopened in April.

As expected, in the wake of the *CAPP v. Rank* decision in California last June, psychologists are aggressively pursuing legislation on hospital privileges in other states, including Massachusetts, New Hampshire, New Jersey, Ohio, and Texas. We are working with these and other district branches to ensure that sufficient information is provided to the legislatures.

The final report on the Harvard University Phase II Resurvey of Psychiatry, prepared by William Hsiao, Ph.D., was published in January. This study related to the Resource-Based Relative Value Scale. The APA work group, chaired by Dr. Donald Scherl, reviewed the report and concluded that it was a major improvement. While we remain concerned about some of the methods, the report does respond to the many questions raised by APA. On average, the relative work values for psychiatric services are 10% higher in the Phase II study than the estimates provided in Phase I. However, these values were only one variable in an equation that will determine Medicare reimbursement beginning in January 1992. Unfortunately, HCFA figures were quite different. At the time of the writing of this report, many questions still remain. APA staff is actively engaged with HCFA in attempting to rectify the disparity.

In February, the Physician Payment Review Commission met in Washington to finalize its 1991 report. APA staff learned that the commission was recommending that clinical psychologists be redefined as limited-license practitioners (they currently are defined as nonphysician providers) and that they be reimbursed at the same rate as physicians. An extensive educational effort, highlighting some of the differences between psychiatrists and psychologists, resulted in changes in the final report, which recommends that clinical psychologists retain their current classification as nonphysician providers and receive an as yet undetermined percentage of the Medicare reimbursement paid to physicians for services they both provide. Our colleagues at the AMA were most helpful in providing this information to members of the Physician Payment Review Commission.

The 1991 Federal Legislative Institute was held March 10-13 in Washington. Senator Pete Domenici, a highly effective advocate for research and care of the mentally ill, received the Jacob Javits Award. Senator Tom Harkin and Mr. Ron Brown, chairperson of the Democratic National Committee, were among the featured speakers. Topics included managed care, government control and the practice of psychiatry, and the role of nonphysicians in the delivery of health care. The attendees met with their senators and congresspersons. As always, Mr. Cutler and his staff planned a thoughtful and stimulating institute, with multiple opportunities for interaction.

We have begun work on Mental Illness Awareness Week for 1991. Senator Paul Simon and Congressman Ron Wyden are the lead sponsors. Mental Illness Awareness Week is an excellent example of the best in interdepartmental staff functioning and is the result of yearlong planning. In 1990, we had the most comprehensive and widespread Mental Illness Awareness Week ever. In addition to a Capitol Hill seminar for legislators, the Division of Public Affairs developed an array of public information materials for journalists and clergy, as well as providers and consumers. District branches conducted public information campaigns in almost every state. The Hometown Radio Interviews reached a huge audience. Dr. Harvey Ruben conducted a

special national 3-hour "Talknet" radio program with special guests that included Mrs. Rosalynn Carter, Dr. Benedek, and Dr. Hartmann.

In October, Dr. Lewis Judd resigned as director of NIMH to return to the University of California. Dr. Judd displayed great wisdom and effective leadership, increasing both the funding and the prestige of NIMH and the profession. Dr. Judd, in collaboration with the National Mental Health Association, initiated the National Mental Health Leadership Forum, whose members represent major professional organizations and advocacy groups. This group, in conjunction with the National Advisory Mental Health Council, held town meetings and hearings that effectively addressed needs and stigma and strengthened the planning process for access to and organization of care. Dr. Alan Leshner is serving as acting director of NIMH, and he has appointed Dr. Sam Keith as his deputy. Dr. Frederick Goodwin, administrator of ADAMHA, has initiated an extensive search for a director. We intend to be actively involved in this important process.

Involvement with our colleagues in organized medicine has been strong and steady. In December, the Board endorsed our continuing participation in the Council of Medical Specialty Societies, and Dr. Hanin, Dr. Robinowitz, and I participated vigorously in the meetings of elected and executive officers of member specialty societies in March. We also have held meetings with elected and executive leaders of the American Academy of Pediatrics, the American Academy of Child and Adolescent Psychiatry, and the American College of Physicians. In April, we were distressed to learn of the death, in a plane crash, of Dr. Nicholas Davies, who was president of the American College of Physicians.

APA's representation in the AMA House of Delegates has been forceful. Delegate John McGrath, M.D., and Alternate Richard Steinhilber, M.D., have worked with the Section Council on Psychiatry and with other members of the AMA House of Delegates to support ideas and resolutions. Dr. Steinhilber, through his membership on the Council on Scientific Affairs, has been able to influence areas of AMA scientific investigation. We were pleased that Dr. Douglas Skelton also was elected to that council. The representation of the American Academy of Child and Adolescent Psychiatry in the AMA House of Delegates and APA's representation in the Resident Physicians' Section and Young Physicians' Section have been productive.

While all of APA's suggestions regarding *Physicians' Current Procedural Terminology, 4th edition (CPT-4)* are still to be accepted, our input (with the substantial support of Dr. Tracy Gordy, who was appointed to the AMA CPT editorial board) resulted in acceptance of three new interactive therapy codes for the 1992 CPT-4. We have developed sample vignettes dealing with levels of service for use with the evaluation and management codes, now being reviewed by the editorial board.

The AMA's executive vice-president, Dr. James Sammons, resigned during 1990. Over the years, I was impressed with Dr. Sammons's knowledgeable and strong leadership. Following an extensive search, Dr. James Todd, the senior deputy executive vice-president, was appointed as executive vice-president. I was delighted to be appointed to a special advisory committee to Dr. Todd; this participation allows for considerable ongoing communication and supports the continuation of our positive and effective interactions with AMA staff.

We have been quite successful in our public affairs functions. In his capacity as chairperson of the Joint Commission on Public Affairs, Dr. Harvey Ruben has provided energetic and wise leadership, working with Mr. John Blamphin, who heads our staff division. Collaboration with industry has helped enhance psychiatry's image with other physicians and the public. The joint effort with the Upjohn Company has supported several activities. The third film produced in this venture, "Depression: The Storm Within," premiered at the American Film Institute Theater at the Kennedy Center in Washington on May 1. It has been well received by viewers—psychiatrists, other health and mental health professionals, and lay persons. The other two films and related campaign materials have been designed to convey such messages as mental illnesses are real illnesses that cause pain and disability to millions of Americans; they can strike anyone; they can be diagnosed accurately and treated effectively. The messages also clarify who psychiatrists are and what they do, as well as emphasize the impact of scientific advances.

We also have reached over 3,500 physicians and other health professionals through the workshop on panic disorders. Materials in-

clude an educators' guide to mental illness awareness that suggests curricula, contains camera-ready materials, and suggests local APA contacts. The comic book "Let's Talk About It," designed for junior and high school audiences, has been well received by more than 64,000 teachers and students nationwide. We are now negotiating for a version in Spanish. Similarly, we have distributed almost a million products (e.g., pamphlets, posters, bookmarks) related to the "Let's Talk About Mental Illness" campaign. The Division of Public Affairs has responded to requests for information about mental illnesses and psychiatric treatment and has provided pamphlets on such topics as anxiety, mental illness, depression, and choosing a psychiatrist.

The Public Affairs Network is one of several locally based groups that expand the reach and effectiveness of the Central Office. Others include those involving government affairs, AIDS, economic and aged care, and education—through chairpersons of academic departments of psychiatry and directors of residency training in psychiatry. They have been important in such efforts as Mental Illness Awareness Week and in providing information to Congress and other groups. We now have an experienced network of trained leaders who can communicate effectively with all varieties of media.

I am most gratified with the direction provided by Dr. Allen Frances, chairperson of the Task Force on DSM-IV. During the past year, there has been an extraordinary amount of activity in this area, and the various work groups have been most productive. APA has been the recipient of funding from NIMH and the MacArthur Foundation to support field trials and analysis of data sets. Final criteria for criteria for diagnostic categories will be published this summer in the *DSM-IV Options Book*. Final decisions about criteria will be made when the results of data analyses and field trials are reported from the field become available. The Office of Research has been publication of *DSM-IV Update* and has coordinated a series of columns on *DSM-IV* in the *Hospital & Community Psychiatry Journal*. Dr. Harold Pincus and the staff of the Office of Research have been invaluable in coordinating and supporting these important activities. The process has focused on the best integration of research and clinical directions in nomenclature and diagnosis, and by providing representation and oversight throughout we hope to maintain a high degree of member involvement. The *DSM* process has been pivotal in demonstrating the scientific credibility and reliability of psychiatric diagnosis and has done much to improve psychiatry's image.

In keeping with our increased involvement with colleagues in other medical specialties, we have met with representatives of many of the organizations to discuss adaptation of *DSM-IV* for primary care. We anticipate that a preliminary draft of the primary care version of *DSM-IV* will be available in 1993.

Dr. Pincus and his staff have received much praise for the field for the quality of *Psychiatric Research Report*. This quarterly newsletter provides considerable information about science, education, and educational opportunities, and research programs.

Congratulations also are due Dr. Pincus for his extraordinary efforts in obtaining significant NIMH and foundation funding to support research and field trials related to *DSM-IV* and to a grant from the van Ameringen Foundation for activities designed to improve recruitment, training, and retention of psychiatrist researchers. Additional praise is due Drs. Pincus and Spurlock for their successful planning of a program supported by a grant from NIMH in support of research training for minority psychiatrists.

Drs. John Talbott and Carolyn Robinowitz lead APA efforts (funded by a grant from the Pew Memorial Trust) to support a series of activities aimed at increasing collaboration between academic departments of psychiatry and state mental health programs. Project Director Ms. Ruth Pitlick has developed an excellent newsletter outlining project objectives, future actions, and current successes.

The AIDS Education Project, under the leadership of Ms. Carol Svoboda, has reached over 7,000 psychiatrists and other health and mental health professionals. The excellent educational activities and materials have been well received. The steering committee, headed by Dr. Stuart Nichols and receives staff support from Ms. Deborah Chacha. In collaboration with our Commission on AIDS, chaired by Dr. James Krajewski, the committee has completed an excellent video dealing with attitudes and presenting cognitive information. These efforts have been most important in addressing the problems associated with HIV disorders and the special stigma affecting AIDS pa-

tients. We are actively seeking funds to continue these important educational activities.

The Office of Education has worked with district branches and other organizations to ensure that educational programs are well planned and organized. There has been considerable effort to develop self-learning and self-study materials, as well as formal learning opportunities. Most noteworthy has been the *Psychiatric Knowledge and Skills Self-Assessment Program (PKSAP)*. The final module of the sixth edition was published in 1990, and I recommend it to you as an excellent opportunity to evaluate and update your knowledge at your own pace, at a time and setting of your choice. There is much interest in using PKSAP as a basis for future recertification efforts.

The Office of Education deserves congratulations for completing work on the 1991 *Directory of Psychiatry Residency Training Programs*. This excellent compendium of accredited programs in general and child and adolescent psychiatry contains information on training sites and facilities, number and type of faculty, number and demographic characteristics of residents, required and elective rotations, remuneration and fringe benefits, and a narrative description of each accredited program. Included are sections on how to choose a residency, subspecialty areas in psychiatry, listings of subspecialty training programs, listings of programs offering joint training in psychiatry and another medical specialty, and the "Special Requirements for Residency Training in Psychiatry" ("Essentials").

We also appreciate the special attention and support provided to residents through the Office of Education and, in particular, the efforts of Ms. Keitt in coordinating activities and components addressing resident issues. This work is increasingly demanding and complex, given the growth of resident members in the Association and their increasing presence in its governance structure.

Of our 37,000 members (representing a net gain of 710 members during 1990, for a 2% increase), 6,000 are residents. This year marked the third year of having both a Member-in-Training Trustee and Member-in-Training Trustee-Elect on the APA Board of Trustees, as well as significant active resident participation in the Assembly and area councils. The component for/on young psychiatrists interacts with its companion component of young physicians in the AMA, and it addresses the particular needs and issues related to the practice of younger psychiatrists. The retention of residents following training is excellent, and the Board of Trustees demonstrated awareness of special issues for this population by adopting a graduated dues schedule for the first years after residency training.

The yearly census of all psychiatry residents documents the interest of medical students in the specialty. This year, however, there was another decrease in the number and percentage of medical students choosing first-year positions in psychiatry through the National Resident Matching Program. We will pursue both data and rationale in the upcoming months. It appears that a larger percentage of medical students are avoiding primary care specialties (e.g., general internal medicine, family medicine) and opting for the more lucrative surgical specialties. We also are concerned about the impact of limited funding in academic departments of psychiatry and how that affects medical student education and recruitment. Recruitment and medical student education will be a high priority for our educational components this year. The APA census suggests that psychiatry residents have greater satisfaction with the field; considerably fewer transfer from psychiatry to training in other specialties. This information is supported by an AMA survey that found psychiatrists to be among the most highly satisfied practitioners. Psychiatry residents demonstrate greater interest in combined residencies and in postresidency subspecialty training. The residents themselves are bright and articulate and bring a special vitality to the Association.

Dr. Marta De Lalla has been a most effective Director of the Office of Membership. She and her staff have made a special effort in recruitment and retention of members and maintain a strong working relationship with district branches. They also work to provide the highest-quality communication and services to all of our members. Staff has worked closely with the APA Committee on Membership, chaired by Dr. Donna Norris, to consider carefully demographic and growth patterns of the membership. Our studies of member retention (at all levels) have emphasized the importance of the district branch dues structure in membership stability. We also recognize that some areas of the country (e.g., Area VI) are experiencing a "graying" of the

membership and increasing numbers of members are being elevated to Life status, so district branches continue to provide costly services but without the dues income to support them.

Also gratifying has been the significant number of members who vote in elections for APA officers and trustees. We remain one of the few large national organizations that conducts a contested election with voting open to the entire membership, and our colleagues in other specialties and disciplines continue to voice their amazement that 40% of the eligible members vote in the election. The election process is an enormous task for a group as large as ours, and I am impressed by Ms. Carol Lehmann's careful attention to detail and mastery of the multiple issues that must be considered to assure a fair and accurate election process.

Dr. Spurlock and her staff in the Office of Minority/National Affairs have been active in many areas, providing voice, support, and recognition of issues that affect minorities, other underrepresented groups, and children and families. Their contributions to the residents' fellowship programs have been especially meaningful to these colleagues and to those of us who interact with them. Dr. Spurlock also has been involved in liaison with medical, mental health, and advocacy groups and has been a most effective spokesperson for the Association.

Dr. Allan Tasman is a thoughtful and energetic chairperson of the APA Scientific Program Committee. Under his direction, the program at the annual meeting continues to expand in content and sophistication. There has been greater attention to integrating research findings into the scientific educational program and more emphasis on interactive and participatory sessions for clinicians. The annual meeting is a high point of the year and mirrors directions for the field, as well as being a proactive and integrating force. The 1991 annual meeting theme, "Our Children: Our Future," generated much interest and excitement and was reflected in multiple sessions and formats and more than 100 excellent continuing education courses, many of which were sold out in advance. The Local Arrangements Committee, chaired by Dr. Daniel Winstead, took advantage of the many opportunities in New Orleans to offer an extremely diverse and stimulating leisure-time program. Advance registration for the meeting was higher than anticipated. Joined by members of the Scientific Program Committee and the Local Arrangements Committee, Dr. Tasman has already begun planning for the 1992 annual meeting in Washington, D.C. APA has also begun planning for the 1994 sesquicentennial annual meeting, which will be held in Philadelphia. A staff committee, chaired by Ms. Carol Davis, has been formed and will work with a committee of members to plan significant events related to this celebration.

None of the success of the annual meeting could have taken place without the devoted efforts of the staff. In particular, I would like to recognize Ms. Davis, who has provided oversight and support as well as her special know-how and experience in so many areas; Mr. George Campbell and staff of the Office of Meetings and Exhibits Management have been immensely helpful, and their professionalism has contributed to the positive tone and format of the meeting; and the remarkable organizational efforts of Ms. Cathy Earnest Nash, who heads the Office to Coordinate the Annual Meeting, and her staff result in a smooth, highly organized program. Their creativity, hard work, and resilience enable us to handle this complex, multifunctional, large-scale event in a way that provides opportunity for each attendee to have an enjoyable and useful educational and social experience.

New Orleans also brings to mind the many contributions to the Association and the field of the late Bill Sorum, a beloved past Speaker of the Assembly. His incisiveness, dedication, warmth, and gentle humor earned him the love and respect of his colleagues. In recognition of his many accomplishments, our public symposium "Our Children in Poverty: What of Their Future?" was cosponsored by the Louisiana Psychiatric Association and the Louisiana Mental Health Association.

The 1990 Institute on Hospital & Community Psychiatry was held in Denver in October. The program, chaired by Dr. James Barter, had as its theme "Emerging Issues in Clinical Psychiatry" and included full-day sessions on AIDS, managed care, dual diagnosis, and women's treatment issues. Fourteen allied mental health groups held meetings, and there was a special presentation sponsored by the NIMH Depression Awareness Recognition and Treatment Program. There were 968 registrants, of whom just under 600 paid a registra-

tion fee; 463 were APA members. The participants' high degree of satisfaction reflected the depth and diversity of program content and the opportunities for interaction among attendees and presenters. Plans are nearly complete for the 1991 H&CP institute, which will be held in Los Angeles, Oct. 20-24, thanks to the institute's program committee and chairperson Dr. Harold Eist. A broad range of mental health providers and consumers will be involved in this meeting. We anticipate that the size of the H&CP institute can be expanded somewhat. A program of this quality should have broader recognition and attendance, and we hope to attract 1,500 to 2,000 registrants.

The *Hospital & Community Psychiatry* journal also has grown in quality and stature, and it reflects the scientific directions of the field and emphasizes innovative aspects of clinical care. The creativity of Editor Dr. John Talbott is reflected in the various columns that integrate policy and theory with clinical practicality. The excellent working relationship between Dr. Talbott and Managing Editor Ms. Ted-dye Clayton has been a model of staff and member collaboration. Similarly, the journal provides a positive model of interdisciplinary collaboration.

The *Psychiatric News* Editorial Advisory Board, chaired by Dr. George Tarjan, has been reviewing both the policies and the content of the newspaper. Consultants from other publications (e.g., *American Medical News*) have provided valuable input. Under the leadership of Dr. Robert Campbell, Editor-in-Chief, and Mr. Herbert Gant, Executive Editor, *Psychiatric News* is increasing its emphasis on meeting members' informational needs. Two new sections are planned—one will highlight psychiatrists' accomplishments and interests, and one will contain debates; we also anticipate greater editorial focus.

We are looking forward to the joint meeting with the Caribbean Psychiatric Association that will be held in Barbados immediately after the annual meeting. The scientific program promises to be stimulating, and this meeting offers good opportunities for a broad array of collaborative activities.

Contacts with the Soviet Union this year have been varied and interesting. In late September 1990, a delegation of Soviet psychiatrists sponsored and paid for by the Soviet Union, came to the United States, visiting hospitals and training centers in Pittsburgh, Indianapolis, Chicago, and Los Angeles. We were most pleased that nine of the visitors (plus an interpreter) were able to attend the 1990 H&CP institute. That aspect of their visit, supported by a grant from the Upjohn Company, was particularly useful in beginning scientific and clinical communication. While we should be cautious about activities that seem to support questionable psychiatric practices, at the same time we must work to strengthen the psychiatric knowledge base and care worldwide.

The World Psychiatric Association (WPA) has been attempting to schedule a site visit to fulfill the stipulations of the conditional membership of the All Union Society of Psychiatrists and Narcologists of the USSR, as agreed to at the 1989 WPA meeting. There have been some problems, and thus delays, in arranging the visit by the review committee, although at the time this report is being prepared, negotiations appear more promising.

I have particularly enjoyed being active in the WPA and chairing the work group charged to prepare a new structure for the organization. Our Office of International Affairs has expanded its efforts and gained wide respect under the leadership of Ms. Ellen Mercer, and this remains a source of special pride and satisfaction to me. Ms. Mercer and her staff provide assistance for psychiatrists in this country and abroad on issues related to education, transcultural practice, and care.

My concern continues to be for the field of psychiatry and our patients, and anything that weakens psychiatry in any country ultimately hurts us as a field. It is time to move past debate and to pay attention to the scientific, social, and economic issues that affect care. I plan to work with the staff office and the APA Council on International Affairs to increase the dialogue and educational interactions.

The APA Ethics Committee has been active, especially in addressing changes in the procedures for investigating ethical complaints. Ms. Carol Davis, who provides staff support for the committee, is to be commended for her careful, thoughtful, sensitive, and sensible efforts; we also appreciate the first-rate legal support provided by Ms. JoAnn Macbeth and Mr. Joel Klein. Their workloads have intensified as the demands on the committee and staff have increased in quantity and complexity.

We have been very pleased with the development of the Office of Information Systems. Under the leadership of Dr. William More, we have developed innovative approaches to information services for our members. Our ability to communicate, as well as collect and retrieve information, has expanded immensely. We are very proud of the excellent, user-friendly format for registration for the annual meeting, as well as the ongoing routine work of the Association regarding member communication, dues billing, accounting, and financing. Dr. More, who is nationally recognized as a medical statistician, has been an excellent resource in our information generation and data analysis. He meets the enormously complicated demands of our financial and other needs in a creative and supportive manner. We believe that in the future communication and information will be an increasingly important base of our function.

I am mindful of many members and staff who have devoted their energy and wisdom to integration, coordination, and unity in a very special way. Ms. Jeanne Robb and staff in the Office to Coordinate the Board and Assembly epitomize the many functions carried out within APA. They promote the best in our governance system and ensure strong links between members and staff.

Also deserving of special mention is the sustained, remarkable high-level contribution of Mr. Joel Klein (and other members of the law firm Onek, Klein & Farr). We have found them available to us for many activities. I will touch on Mr. Klein's work on professional liability, but he also deserves praise for his work with our Commission on Judicial Action. Mr. Klein has been a valued friend as well as a counselor through a number of difficult and thorny decision points.

I am most gratified by the creative leadership and energy shown by past President Dr. Carol Nadelson as Editor-in-Chief of *APPI*. In the past year, she has been extremely active not only in broadening and strengthening *APPI*'s ongoing work, but also in outreach to develop strong working relationships with potential authors in this country and abroad. The *APPI* Editorial Board has been broadened to include experts in a variety of clinical areas. Under the able guidance of Mr. Ronald McMillen, *APPI* has begun publication of journals; this expanded effort will provide an opportunity for leadership in such areas as neuropsychiatry, psychosomatic medicine, psychiatric education, and psychotherapy. Our marketing efforts, coordinated by Ms. Karen Loper, have already resulted in new directions and greater income. *APPI*'s staff work in expanding our foreign markets has resulted in new professional and business alliances plus greater opportunities. In its 10 years of existence, *APPI* has become well recognized and highly regarded in the publishing industry. Not only does it have a competitive edge in psychiatric publications, as evidenced by the content of book reviews and by sales volume, but its products also provide an opportunity for scientific education and negation of some of the stereotypes about psychiatry and psychiatric patients.

The crisis in medical liability has been marked by questions about the availability and cost of general liability insurance in this country, which have had a profound impact on many functions and activities. Just a few years ago, we had major problems obtaining needed liability insurance for our members. A separate corporation was formed—Professional Risk Management Services, Inc. (PRMS)—which, by serving as our insurance administrator, provided a vital and cost-effective function for our membership. As a separate and young corporation, PRMS has faced problems in accountability and availability of insurance for all members, and it has dealt with questions about issues specific to members in such areas as administration and general medical care.

Last year, we sold our share in PRMS after careful review and consideration of the legal, fiscal, and service considerations. By not being bound to PRMS, while still maintaining control of the APA Insurance Trust and risk management policies, we can make strong demands for excellent service and are free to negotiate with PRMS or other administrators for our programs. The APA Insurance Trust remains unchanged, as does our participation in the various policy and procedural aspects of rate setting and risk management. We are better able to protect our members while ensuring the availability of the most cost-effective insurance programs. Special acknowledgment must be provided to Mr. Klein and Ms. Macbeth of Onek, Klein & Farr; Dr. Alan Levenson, chairperson of the Board Committee on Insurance; Dr. Robinowitz; Mr. Rich Feeley, our staff insurance and financial consultant; and the APA members involved in the membership insurance

committees for their extraordinary endeavors in support of our insurance activities. Our success has been vital to our members' practices.

For our insurance program to be successful and meet members' needs, we must constantly deal with the interface and conflict between functioning as a member organization and as a business. While we have to be sensitive to all of the issues and problems practitioners have in dealing with the threat of liability suits, we also have to base the program on a sound fiscal footing and avoid adverse selection. We do offer the best program for meeting members' needs, with more provisions for member choice and control in case settlement. Unlike most commercial carriers, we do not cancel coverage on the basis of suits brought or claims made. Further, the "profit" goes back to the membership in the form of lower premiums, rather than to stockholders. We also are offering on a pilot basis a "claims made" policy that may be useful for younger members just beginning practice or those who plan on a stable practice for some time.

Special note also should be made of the contributions of Ms. Elizabeth Thomas who, in addition to her role as Assistant Director of the Office of Membership, serves as the ombudsperson for APA members in insurance-related matters. Ms. Thomas has developed a strong working relationship with PRMS and has been extraordinarily helpful in addressing and solving problems of communication and information. Through her efforts and those of Mr. Feeley, the number and intensity of complaints related to insurance matters have fallen considerably.

Business ventures demand both substantive knowledge of issues affecting our members and their practices and a sound fiscal structure. Dealing with tight budgets, the recession and a leveling off of income, and prudent planning for the future financial strength of the Association has been a monumental effort, demanding considerable member and staff coordination and proactive planning. I am especially grateful to our Treasurer, Dr. Mary Jane England, the chairperson of the APA Budget Committee, Dr. Donald Scherl, Mr. Feeley, and the many members who have played key roles in ensuring income for the Association and regulating our expenses. Dr. Robinowitz, Dr. Jack White, Mr. Robert Milanicz, and the staff involved in financial planning and budget implementation also have done an excellent job not only in planning and execution but in dealing with the many individual needs generated by fiscal restraints.

Mr. David McClanahan has contributed strongly to the smooth day-to-day functioning of my office. Ms. Katherine Chambless has

been a marvelous addition to the team. Dr. Robinowitz also has been pivotal in this integrative effort, which, in my judgment, shows APA at its working best. Further, Dr. Robinowitz has consistently taken on increasing responsibilities in all areas of Association functioning and has performed magnificently. As far as I am concerned, our working partnership in day-to-day and long-range management is excellent.

Of vital importance is the presence of a largely behind the scenes staff member who takes major responsibility for making it all happen. Ms. Carol Davis oversees the functioning of my office and all its related events while at the same time maintaining major staff support responsibility for the demanding work of the Ethics Committee, the Ethics Appeals Board, and the AMA. She has a special ability to develop and implement planning processes and is an extraordinarily knowledgeable and sensitive resource. The nature of her work is such that she rarely receives public attention or recognition. Yet her contributions are invaluable, and she has won the trust and respect of us all.

Comments about "the best in the APA" are a good link to my belief that we have been extremely fortunate in our choice of leaders. Our President, Dr. Elissa Benedek, has been outstanding; her knowledge, vision, concern, and effectiveness have had a major impact on our functions and our future. Her thoughtful guidance and her concern for patients, children and their families, science, education, and patient care have strengthened the Association and the field. Our Speaker, Dr. Edward Hanin, also has been outstanding. His sensitivity to and knowledge of Assembly moods, directions, and needs, his thoughtful consideration of issues, his remarkable ability to work closely with members and staff, and his warmth and caring have made him especially effective for the Assembly and the Association. It has been a privilege to work with all of our members this year toward a stronger and more effective APA, and I anticipate an excellent alliance with our incoming President, Dr. Lawrence Hartmann, the next Speaker, Dr. Thomas Pfahler, and all the other APA members who serve the Association and the field so ably.

Extensive reports on the individual staff departments are available from the Central Office. They attest to the diversity, enormity, and complexity of staff efforts and demonstrate our commitment to strengthening the field and supporting our members and the patients they serve. It is a privilege and pleasure to be Medical Director of such a strong and vital organization.

Report of the Speaker

Edward Hanin, M.D.

It has been just a year since I sat down to write my Speaker-Elect's report, but what a year it has been. At that time, we were celebrating the end of the Cold War. Major changes were underway in Eastern Europe. The Berlin Wall was down. A new era was dawning in the Soviet Union. The "peace dividend" was finally going to free up funds to address the rather large tears in the safety net of services available to those in need. Who would have predicted a war in the Middle East between Iraq and ourselves, the ethnic turmoil in Eastern Europe, the political regressions in the Soviet Union?

As psychiatrists, we recognize both the very human need to plan out our lives and control our destinies and how often the unpredictability of life destroys our illusions. This recognition has been powerfully brought home to me this year, both personally and in my office as Speaker. It has provided a stimulus for this report to the membership at the end of my year as Speaker.

The Assembly has lost two of its members, suddenly and unexpectedly. Dr. Jose Arana had just joined the Assembly as representative from the Hispanic caucus. He was an eminent psychiatrist at the University of Maryland, and his death at the age of 46 prematurely ended a distinguished career.

The death of Dr. George Ginsberg, Area II representative, was a profound shock to his many colleagues, both in and out of the Assembly. George and I worked closely together in Area II and in the Assembly. He was a good friend, the kind of friend one can ill afford to lose. The profession has lost a distinguished leader, medical education a true champion, and all of us who knew him, a physician and colleague of immense integrity and breadth of vision. His work with the Members-in-Training in the Assembly should especially be noted. The vital role they have assumed in the Assembly is a tribute to his efforts. He will be truly missed.

Although life may be unpredictable at times, this does not relieve us of the necessity of planning for the most likely eventualities. An individual who has no goals, no priorities, no responsibilities, no concerns for others, who drifts here and there with no focus, would hardly be held up as a paragon of mental health. Indeed, we might strongly consider a *DSM-III* diagnosis appropriate. So it should be with an organization. The mission of that organization should be clear. Long-term goals need to be in place, as well as strategic plans to achieve those goals. These plans must include an assessment of the fiscal impact of these goals, and their achievement must be measured against these fiscal realities and appropriate priorities set. APA has, to my mind, been justifiably criticized for its lack of long-range planning, its difficulty in setting priorities, and its tendency to be more reactive than proactive. When times are easy, these lacks are easy to overlook. When money flows easily, there seems to be no need to prioritize. But money no longer flows easily; not in health care, not to our members, not to their patients, and not to APA. APA will need to make difficult choices, will need to set priorities, and will need to choose between options that are not necessarily good or bad but may both be desirable.

Decisions as to where to put our efforts will need to be based on judgments about which items on APA's long agenda are most likely to move at a particular time. Positions and goals must be specific enough to give us direction but not so rigid as to not permit us to take advantage of unexpected opportunities or to avoid unanticipated obstacles.

The issue of access to care, with all of its complexities, provides us with a good illustration of this dilemma. Roughly 37 million Americans do not have adequate health insurance. Others do not have access to adequate or appropriate psychiatric care because of discriminatory coverage. Still others find their access to services limited because of the egregious case management practices of some managed care companies. Where should APA be placing its efforts? Should our efforts be directed toward influencing national legislation on universal access and assuring the inclusion of psychiatric services in the basic benefit package? Should we concentrate on obtaining state mandates for non-discriminatory coverage? Would efforts to better regulate managed care practices be the way to go? Ideally, we would like to attend to everything, but perhaps we cannot and will have to choose. Toward what ends should our efforts to control the negative impacts of managed care be directed? Should we be looking to the building of coalitions with other specialties and, perhaps, even with psychology? How important will it be to develop practice guidelines and utilization review standards? Can we collaborate with large employers who, while seeking to control costs, really want to provide good care for their employees? Can we realistically do everything? Probably not. Are we comfortable in choosing among options? Not really. Do we have to? I believe so. The California Psychiatric Association saw an opportunity to gain nondiscriminatory coverage for a portion of patients, those with "biologically based illnesses," providing that it was willing to accept case management of care as part of the package. Should it have said "No" because the plan did not include all patients or because psychiatrists would need to find ways to effectively work with case reviewers and managers? I do not think so.

While APA needs to be able to move quickly in a rapidly changing environment, such a need should not be an excuse for inadequate planning, hasty and thoughtless decisions, or limited input from the membership. For example, I believe that our Board of Trustees showed great wisdom in asking for the widest possible member input on strategies to affect managed care. I was most impressed with the responsible way in which the district branches provided that input and with the quality and maturity of their recommendations. We need to find some way to institutionalize this kind of process. Networks may be a partial answer. They have shown promise in the areas of legislation and public affairs. A similar network relating to managed care issues is being developed. Networks are very useful in providing for a two-way flow of information early on in a process. They are, however, very costly to operate, and their development would need to be limited to issues of the highest priority.

The Assembly has become an increasing force in APA policy development. It has become an even more effective deliberative body. The increased role assigned to the Assembly Executive Committee has permitted it to act for the Assembly between meetings and to coordinate information flow to and from the area councils.

The Assembly has developed mechanisms for the rapid review of codes for the *Physicians' Current Procedural Terminology, 4th edition (CPT-4)* and will move rapidly to consider practice guidelines. However, for the Assembly to become even more effective, we will need to streamline the way information and actions flow between it and the councils, commissions, and other components of APA. That flow can and should be better, and I hope that efforts will be made to look at this issue and to come up with recommendations for the Assembly to consider.

This past year as Speaker has been a wonderful and exciting year for me. I have learned so much. I have had the opportunity to travel around to the area councils and meet with district branch leaders. How fortunate we are to have so many able people willing to work so hard for the benefit of their patients and their profession. We have such a wealth of talent in the Assembly. Members do their homework, draw on the expertise of their colleagues in the district branches, and vigorously debate all issues. Anyone who reviews the minutes of an Assembly meeting will be impressed with both the breadth of the issues discussed and the quality of the debate. The effectiveness of members of the Assembly has been recognized, and the Assembly has become an increasingly important element in APA governance. It has been an important factor in the development of strategies on managed care, practice guidelines, liability insurance, subspecialization, and the many other areas where joint Board-Assembly activity has become the rule rather than the exception.

The Assembly is a dynamic body, seeking to adapt its functioning to the changing face of American psychiatry. Structural changes have come more slowly, but I know that the Assembly will do what is needed to perform its role well and responsibly. The Assembly's Committee on Planning, under the able leadership of its chairperson, Dr. Ronald Shellow, has contributed significantly to this growth and development.

The Assembly Executive Committee has provided creative leadership, both for the area councils and for the Assembly. Several years ago, the Assembly decided to give broader powers to its area representatives who make up the Executive Committee. Our current group of area representatives demonstrate what a wise decision we made. The area councils have never worked better, not only as discrete units but in the way in which they collaborate with each other. No one who has not been Speaker can realize how dependent the Speaker is on his Executive Committee. They are the ones who really make the Assembly work.

I have to say a special "thank you" to my parliamentarian, Dr. Robert J. Campbell. Dr. Campbell is a distinguished past Speaker and past Vice-President of APA. Only he knows how many times he saved me from disaster—and he is much too discreet to tell. He has truly been of tremendous help, and I am both pleased and honored that he was willing to return to the Assembly during my year as Speaker.

Dr. Jack McIntyre and Dr. Gerald Flamm, my two immediate predecessors as Speaker, have been of tremendous assistance. They have chaired important committees of the Assembly and have been vital to its smooth functioning. I hope I can be as useful to my successors as they have been to me.

The Speaker-Elect and the Recorder, in addition to all their other functions, are the eyes and ears of the Speaker. They provide both an early warning system as to potential problems and excellent advice and counsel. Dr. Thomas Pfahler and Dr. Ronald Shellow have been invaluable to me during my year as Speaker. Dr. Pfahler's activities have done much to put the Assembly on a sounder financial footing. He has been a vital and eloquent second voice for the Assembly on the Board of Trustees. We will be in very good hands next year under his leadership. Dr. Shellow's important role as chairperson of the Committee on Planning has already been mentioned.

Dr. Irvin M. Cohen, our most senior past Speaker, deserves special mention. Dr. Cohen has been a member of the Assembly for 25 years. What a record of dedicated and distinguished service to the profession. He was Speaker-Elect when I first became my area's representative. He has been a source of great support and valuable advice, and his role has been a true model of what a dedicated practitioner can bring to APA. He will be leaving the Assembly this year, and we shall all miss his integrity, his good sense, and his devotion to the Assembly. We will also be losing the best audience for a good joke in the entire Assembly. Dr. Cohen has long been the member of the

Assembly to whom we turned when we wanted someone with the trust of the Assembly members to chair an important task force. Most recently, he was asked to take on the difficult and challenging task of leading the Assembly's review of APA's professional liability program. He did a marvelous job and brought this effort to a very satisfactory conclusion. He will truly be missed. Fortunately for me, I serve with Dr. Cohen on other APA components, so I will still reap the benefits of his wisdom.

In my report last year, I commented on how impressed I was with the quality and dedication of the APA staff. Now that I complete my year as Speaker, I am even more impressed and I appreciate, as I could not have a year ago, how important they are to the functioning of the organization. No Speaker's report could be complete without many words of thanks to Dr. Melvin Sabshin and Dr. Carolyn Robinowitz, our Medical Director and his deputy. I have never called for information and not gotten it. I have never asked for advice and not received a thoughtful reply. They have been there to provide guidance and support, when asked. They have been most sensitive to the need to keep APA officers well informed, while not in any way trying to direct or alter my decisions. They have presented options that I would not have considered and have been invaluable to me during this year. We are very fortunate to have physicians of this stature working for our professional organization. We are the envy of many other professional groups.

My thanks extend to the other Deputy Medical Directors as well. Dr. John Hamilton, Dr. Harold Pincus, and Dr. Jeanne Spurlock have been of great help to me as the Assembly has dealt with issues in their areas of responsibility. I am most grateful to them for their patience as they have had to bring me up to speed in areas they know so well. Mr. Jay Cutler, and indeed the entire Division of Government Relations, are a very valuable resource. We need to listen to what they say. It is not always what we want to hear, but no one could be more accurate judges of the attitudes of government, and we are very lucky to have them on our side.

Other departments have also made substantial contributions to the

effectiveness of the Assembly. If I listed everyone, this report would go on much too long, but I am grateful to them all. A very special expression of appreciation and thanks has to go to those staff who support the Board and Assembly. Without them, the Assembly literally could not function. Mr. Michael Murphy, Ms. Lea Mesner, Ms. Carol Lehmann, and Ms. Elisabeth Fitzhugh all provide superb support to the Assembly. They have put up with frequent calls from the Speaker and have been of great support.

All of you who work in the Assembly or have been active in your district branches know what a special person Ms. Jeanne Robb is. She has been invaluable to me during my year as Speaker. She was always there, always ready to provide the information needed, always ready to provide support, and, perhaps even more important, always willing to say "No, don't do that," when I was heading off in the wrong direction. This has not been an easy year for Jeanne. I only hope that my demands on her did not add to her difficulties. She certainly made my year much easier. I value her as a colleague and a friend.

APA has been blessed with a series of dynamic and effective leaders. None has been more effective than our President, Dr. Elissa Benedek. The President and Speaker work closely together throughout the year. I have learned an enormous amount from that contact. Dr. Benedek's skill in leading without domineering, in being able to draw the best from her colleagues in difficult situations, and in being able to move an agenda while allowing full and free discussion has been truly remarkable. She has been a lucid, effective spokesperson for psychiatry. It has been a true privilege to work with her and to learn from her. I am most grateful to her for all she has done for me personally, for the Assembly, and for the Association.

I am honored to have been the Speaker of the Assembly of the American Psychiatric Association. Psychiatry is a wonderful profession. Having this opportunity to associate with so many wonderful colleagues has been a marvelous experience. I look forward to working with the new leaders as they take on the many issues facing our field. I know we are in good hands.

Report of the Speaker-Elect

G. Thomas Pfaehler, M.D.

INTRODUCTION

The year spent as Speaker-Elect of the Assembly is at once a sobering and exciting time. The new Speaker-Elect is cordially welcomed and immediately immersed in the obligations of the Assembly and the Association, beginning with meetings of the Joint Reference Committee and Board of Trustees in June following the elections at the May Assembly meeting. The Speaker-Elect is, by virtue of the office, the vice-chairperson of the Joint Reference Committee, a member with voice of the Board of Trustees, an invitee to the annual officers meeting, and a welcomed partner of the President-Elect in filling many positions in multiple councils and components. It is clear that the voice of the Assembly is heard throughout the Association and its opinions are actively sought. The weight and responsibility of this level of involvement is surmounted only by the excitement and pleasure of working with many highly qualified and dedicated colleagues.

In addition to the ex officio positions, I have had the pleasure of continuing several other obligations as the Speaker-Elect, not the least of which is acting as chairperson of the Assembly Budget Committee. I have continued as the chairperson of the Assembly Committee on APA Fiscal Policy and, thus, as an invitee to the meetings of the con-

stitutional Budget Committee of APA. More recently, I have been asked to become an interim director on the board of the foundation established by the Association to facilitate the development of external financial resources to further APA's mission and goals. Most recently, the current Speaker has asked me to chair a task force to develop a "managed care" strategy on behalf of the Assembly of District Branches. These activities have given me insight into both the basic fiscal workings of the Association and an appreciation of the care, concern, and dedication exhibited by colleagues who have been carrying out the functions of these committees on behalf of APA. I have developed an acute awareness of the sensitivity necessary to represent the Assembly and the membership in such areas as the acquisition and disbursement of nondues revenue of the Association. It is clear that such revenues must be developed if the Association is to grow but that they must also be managed so they do not present conflicts of interest or inappropriate obligations.

Perhaps the most important realization to come from my experience has been that APA must develop a strong participatory planning system. The current fiscal crisis has made it clear that the Association must be ever aware of its mission, goals, and objectives. Decisions about expenditures of resources and the setting of priorities among the functions of the Association must be consistent with the future

health and proactive functioning of the Association and must be made on behalf of all of its members.

EVOLUTION OF ISSUES FACING THE ASSOCIATION

It seems clear that APA has been evolving in many areas. While it maintains as its highest priority excellence in diagnosis and treatment of patients with mental illness and developmental disabilities, along with preservation of the highest professional and academic standards for psychiatry, the Association has increasingly become involved with issues that directly impinge on the personal practices and concerns of its members. This evolution requires both a responsiveness and an unusual sensitivity to the membership on the part of Association leaders to preserve the unity of voice necessary to the professional integrity and excellence characteristic of psychiatry over the decades. Some of the issues that must be melded with the priorities reflected in APA's mission and goals are as follows.

1. The Association has become involved with the provision of professional liability insurance to its members. No member may practice conscientiously without such protection. APA's efforts in this direction must take into account the need to maximize the participation of the membership in its liability insurance program, as well as the realities of the insurance world.

2. The Association has recently been integrally involved in quality assurance through its functioning as a contracting reviewer for the CHAMPUS program. APA must clearly learn from this experience about the effect of such activities on the autonomy of its members. It must recognize the kind of accountability and close scrutiny of clinical activity necessary to support members' claims of professional integrity and expertise. Above all, equity of service and access to service for psychiatric patients must be preserved.

3. The recent establishment of a foundation to increase the availability of financial resources for APA presents significant challenges. Raising funds effectively must be an intensely personal undertaking if it is to be successful. The priorities for the solicitation and disbursement of such outside funds must be made with input from the membership so as to protect their consistency with the mission, goals, and objectives of the Association.

4. The recent launching of the project to establish practice guidelines for psychiatry clearly has a major impact on the practice of all APA members. While such necessary systematization of psychiatry seems unavoidable, clearly the expertise available to APA must be supplemented with education and input from the membership.

5. The development of more clearly representative service codes for inclusion in *Physicians' Current Procedural Terminology, 4th edition (CPT-4)* affects the membership's ability to receive fair and adequate compensation for the services and responsibilities they undertake in treating their patients. It also directly affects the equitable provision of services to all patients suffering from mental illness or developmental disabilities.

6. The relatively new concept of managed care clearly affects all psychiatric practitioners. It is essential that the Association foster the most complete education possible of its membership regarding the difficult decisions involved in the assessment and management of care provided to our patients. Closely coordinated with the development of practice guidelines, this area deserves APA's greatest efforts to develop high standards so it is clear to anyone undertaking such management that lesser priorities will not be accepted.

7. The Association continues to revise and improve its *Diagnostic and Statistical Manual of Mental Disorders*. This publication has for years been the benchmark for all mental health professionals, providing a widely read and respected taxonomy of the mental illnesses with which we deal.

8. The Association has become involved actively with the American Board of Psychiatry and Neurology regarding recertification. While quiescent for periods, this issue remains a clear challenge to our members to demonstrate their continued professional development, dedication, and responsibility.

9. The Association has recently had major input into the development of the Resource-Based Relative Value Scale as a mechanism to attempt equitable reimbursement on behalf of our patients by the insurance programs of the federal government. The Association must

continue to emphasize quality of care while assisting in determining a reasonable assessment of the resources necessary to provide equitable care to our patients.

10. The Association has carried on active and ongoing efforts to see that the psychiatric services received by minority populations in the United States are equivalent to those provided to the majority. Internally, the Association has struggled long and hard to achieve equitable representation of its members belonging to these minority groups. These efforts must continue if the Association is to maintain its credibility in an increasingly pluralistic society with rapidly growing minority groups.

11. The division of psychiatry into subspecialties with individual recognition and routes to certification has provided APA with a significant challenge over recent years. It is essential that the Association continue to carefully examine the delineation of such subspecialties to assure that our colleagues with special areas of expertise receive the recognition and certification they need. It must, at the same time, continue to preserve the unity among psychiatric subspecialties and take care not to allow the development of a many-tiered system in which some of our patients will be denied specialized services because they are delivered by qualified general psychiatrists rather than certified subspecialists.

EVOLUTION OF THE ASSEMBLY OF DISTRICT BRANCHES

While the evolution of the Association as a whole has been to the entry into essential and strategic areas closely bound to the interests of our membership, as I have discussed, APA has also experienced an internal evolution both of the Assembly and of the relationship between the Assembly and the Board of Trustees.

The Assembly continues to struggle with representation. Thus far, it seems as though geographic representation provides the most satisfying system and assures, as much as possible, that the voices of all members will be weighed equally. While doing this, however, the Assembly must face the challenge of somehow recognizing different practice styles, different characteristics, such as minority status and age, and different subspecialties within psychiatry. Clearly the establishment of minority representatives and the inclusion of Members-in-Training as active participants in the Assembly process represent evolution in this direction. The multiple joint memberships held by members of the Assembly in other organizations permit some representation of subspecialties and practice styles.

The Assembly Executive Committee has also evolved—now can competently synthesize and expedite actions of the Assembly in such a way as to assure representation of the will of its members and district branches. It provides a key mechanism for briefing the leaders of the Assembly area councils so that they may continue their excellent leadership and inform the members of their councils in a competent and competent way. The establishment of the Assembly Executive Committee's executive session mechanism to allow complete communication regarding sensitive issues is a part of this evolution. It is clear that the privilege of executive session is not designed to sanction secret action by the Assembly Executive Committee. It is rather, as I described, essential to the thorough briefing of Assembly leaders on sensitive issues so they may provide competent leadership to area council members and thereby to members of the district branches.

Complementary to the evolution of the Assembly Executive Committee has been the evolution of the area council structure within the Assembly. There has been a remarkable increase in both the expertise in the area councils and a maturity in the debate. This has made it possible for the Assembly to deal in a constructive and admirable way with many complex issues. The Assembly of District Branches, by virtue of its numbers and the length of time it spends in session either as area councils or as the full Assembly, provides a significant complement to the Board of Trustees, which maintains the ultimate fiduciary responsibility on behalf of the membership. It is essential that the area councils and the Assembly as a whole maintain the ability to debate issues and formulate proposals so that the Board of Trustees can carry out its fiduciary and corporate responsibilities with the benefit of the Assembly's contributions.

Yet a fourth evolution has been the Assembly's move into the direction of anticipatory planning regarding issues and functions of the As-

sembly Committee on Planning continues to meet regularly, and its meetings provide an excellent opportunity to discuss issues in a proactive manner before they reach the Assembly. A most significant opportunity is the chance to develop a true proactive planning process for the Assembly and, subsequently, through the relationship with the planning committees of the Board, for the Association as a whole.

The Joint Reference Committee met together with the Assembly Executive Committee for the third time in the winter of 1991. The evolution of the relationship between representatives of the Assembly and representatives of the councils and components has been furthered by the activities of the Joint Reference Committee's chairperson, the President-Elect, Dr. Lawrence Hartmann. The potential for further evolution in the councils and components, and the Assembly's ability to represent the membership as a whole, through education and debate, will be a pleasure to see.

Finally, the Board's recognition of the Assembly is nowhere better represented than in the increased use of jointly appointed commissions and task forces to deal with issues that are essential to the functioning and survival of the Association. The ongoing Joint Commissions on Public Affairs and Government Relations are clear examples of this. Their achievements in presenting the public face of psychiatry and its relationship to the federal government and local governments are indeed impressive.

In sum, the evolution of the aforementioned functional units of the Assembly of District Branches provides an effective way to avoid what a political science colleague of mine describes as the "iron rule of oligarchy." In simple terms, the sheer magnitude and complexity of the issues confronting APA make the efficiency and speed of decision making by a small group of intimately and intricately involved members very attractive. A responsible and efficient process in the Assembly of District Branches provides the necessary counterbalance to this to assure that the widest possible representation of membership needs and preferences is included.

CENTRAL OFFICE EVOLUTION

APA, like other associations that must deal with complex and manifold issues, has become extremely reliant on its staff. The care and feeding of this staff is an extremely important issue for the Assembly and the Board of Trustees. The expertise of individuals in the offices for government affairs, public affairs, coordination of the Board and Assembly,

economic affairs, education, and resource development must be used efficiently. The excellent personnel in these offices require strong planning by the Assembly and Board and clear direction so as to assure their efforts and presentations represent APA as a whole and its obligation to patients with mental illness and developmental disabilities. The cost of maintaining these offices is far and away the largest ongoing cost facing the Association. Such staff reliance is essential to the functioning of the organization but must be coupled with detailed planning and direction in order for APA to function at its best. This requires a balance between the autonomy consistent with the high level of expertise and competence possessed by staff members and the necessity of working together in an integrated fashion, always within the mission and priorities of the Association.

PERSONAL EVOLUTION

In closing, I wish to recognize many people who have been useful, supportive, and encouraging to me during my time with the American Psychiatric Association and the Assembly of District Branches. I know full well, however, that such a list would take several pages, and clearly such a complete undertaking would inevitably leave someone out. I will, therefore, take the personal privilege of thanking just a few individuals with the full understanding that many others deserve such thanks and recognition as well.

Most important, the small group of past Speakers, including Dr. Edward Hanin, Dr. Gerald Flamm, Dr. John McIntyre, and Dr. Irvin Cohen, have continued to be supportive in this Speaker-Elect year. I trust that I will be able to count on them as a source of advice and support during the coming year. I view this as essential to the continuity of leadership in the Assembly.

I would also like to recognize Mr. Michael Murphy, Ms. Lea Mesner, and Ms. Jeanne Robb as representative of the support staff for the Board and Assembly. Their availability and willingness to provide context and continuity to a new officer is indeed appreciated. They have a wisdom that comes from ongoing involvement with and dedication to the Association.

Finally, it is my goal and objective during my year as Speaker of the Assembly to attempt to strengthen the Assembly structure and facilitate its voice on many of the issues into which APA has been catapulted. I hope to leave the Assembly a bit further along the evolutionary path I have described and appreciate the opportunity to serve.

Report of the Committee on Constitution and Bylaws

William B. Spriegel, M.D., Chairperson

The Committee on Constitution and Bylaws this year accomplished its work by telephone conference call and mail ballot, and I am indebted to the members of the committee for completing its business so expeditiously. They include Drs. Gerald Sarwer-Foner, Henry Payson, Richard Thurrell, Walter Shervington, Naomi Goldstein, and Lee Park, Assembly liaison. The committee was ably assisted by Ms. Carol Lehmann of staff.

The committee acted on several matters referred to it by the Board of Trustees and proposed amendments to implement recommendations that had originated in the Committee on Membership, the Nominating Committee, the Elections Committee, and the Assembly. The proposed amendments would 1) modify the dues-exempt status of members who reach Life status in 1993 and thereafter, 2) add a member of a minority or underrepresented group to the Nominating

Committee, and 3) increase the number of signatures required for nomination by petition.

The Board approved all amendments for reading to the membership at the 1991 annual meeting and placement on the 1992 ballot. The text of the amendments follows.

In keeping with its responsibilities as outlined in the "Operations Manual of the Board of Trustees," the Committee on Constitution and Bylaws agreed that at one of its future meetings it should systematically review the entire Constitution and Bylaws to identify possible conflicts or ambiguities in wording and to make recommendations to bring it into conformity with current practices. The committee also requested the Board to establish the policy that whenever feasible a member of the Committee on Constitution and Bylaws be included in substantive discussions in any component

regarding changes that might lead to amending the Constitution and Bylaws.

PROPOSED AMENDMENTS TO THE CONSTITUTION AND BYLAWS

The following amendments were approved by the Board of Trustees in December 1990 and March 1991 for reading to the membership at the 1991 annual meeting. The amendments will be disseminated to the membership not later than January 1, 1992, and will appear on the 1992 ballot. In the text that follows, brackets indicate deletions and bold underscoring indicates additions.

Proposed Amendment 1

Changes to chapters 1.13 and 8.6 would remove the dues exemption of members who achieve Life status according to the rule of 95 in 1993 and thereafter and would require them to pay two-thirds of the usual dues during their first 5 years after achieving Life status and one-third dues during the second 5 years. The dues exemption of members with Life status prior to 1993 would be continued.

Chapter One. Members

13. Inactive members of any category shall be those whom the Board has, for sufficient reason, excused from paying dues. Members of any category who are placed in inactive status shall be excused from paying dues and shall not receive credit toward the [95 years' dues exemption formula] number of years of active membership required for Life status for those years of inactive status. Active members may be granted waiver of dues by the Board for sufficient reason, and such members shall receive credit toward the [95 years' dues exemption formula] number of years of active membership required for Life status for those years the members are in the dues waiver status.

Chapter Eight. Privileges and Responsibilities

6. Every Fellow, General Member, Associate Member, and Member-in-Training shall pay both dues and assessments as determined by the Board and the District Branches. Medical Student Members shall pay a one-time, national membership dues. Life Fellows, Life Members, and Life Associate Members who achieve Life status in 1993 and thereafter shall pay two-thirds of the highest dues rate during the first five years after reaching Life status, and one-third of the highest dues rate for the second five years. Thereafter, Life Fellows, Life Members, and Life Associate Members shall be exempt from paying dues.

All other categories of membership, including those who reach Life status prior to 1993, shall be exempt from paying dues and assessments to both the Association and its District Branches. [A dues-paying member shall be exempt from paying such dues and assessments when the sum of the member's

years of active membership in the Association plus the member's age at the start of the fiscal year shall equal 95.] All dues exempt members, however, shall pay for subscription to publications at a reduced rate as determined by the Board if they desire to receive them.

[Such dues] Dues will include amounts allocated to subscriptions for the *American Journal of Psychiatry* and the *Psychiatric News*. The membership application shall contain a provision for allocation of a specific portion of the dues to pay the cost of periodical subscriptions to these publications. [Dues exempt members shall pay a reduced subscription rate for these publications if such members desire to receive them.]

Proposed Amendment 2

This amendment would expand the Nominating Committee to include a representative of a minority or underrepresented group, who would be selected in a manner similar to the way area representatives to the committee are chosen.

Chapter Six. Councils, Committees, Boards, and Other Organizational Entities

5. The Nominating Committee shall be appointed by the President within the first sixty days of his or her term of office and shall be comprised of a representative from each geographical area of the Assembly and a representative from Minority/Underrepresented groups plus a chairperson. Each Area Council shall propose at least three candidates, and the Assembly Committee on Minority and Underrepresented Groups shall propose at least three candidates, and the President shall appoint the members from among those candidates. The President may choose any voting member as chairperson of the Committee. The Committee shall nominate at least two candidates for each office and report its nomination to the Board by September 15 or a September Board meeting, whichever is later, for immediate dissemination to the members.

Proposed Amendment 3

This amendment would increase the number of signatures required for nomination by petition from 200 to 400 for national offices and from 50 to 100 for area trustees.

Chapter Nine. Voting

1. Nominations for national office except that of Area Trustee shall be made by: (a) the Nominating Committee; or (b) a petition signed by [200] 400 or more members eligible to vote. Nominations for Area Trustee shall be made by: (a) procedures established by the Assembly; or (b) a petition signed by [50] 100 or more members of that Area who are eligible to vote. Nominating petitions must be filed with the Secretary by November 15 of the year immediately previous to the year in which the nominee would be elected.

Report of the Committee on Membership

Donna M. Norris, M.D., Chairperson

The Committee on Membership met on Nov. 6–9, 1990, in Washington, D.C. Present were Drs. Donna M. Norris (chairperson), Jack W. Bonner III, Fernando J. Cabrera, James M. Campbell, Siobhan Coomaraswamy, Lois B. Fuller, Rodrigo A. Munoz, A. Granville Tolley, Michael J. Vergare (consultant), and Aron S. Wolf (Assembly liaison); Dr. Marta De Lalla, Director of the Office of Membership; and Office of Membership staff. Guests present were Dr. Melvin Sabshin, Medical Director; Dr. Carolyn B. Robinowitz, Deputy Medical Director; Dr. Harvey St. Clair, chairperson of the Resource Development Committee; Dr. Jane Wells, Committee of Young Psychiatrists; Mr. Richard Feeley, APA consultant; and Ms. Andrea Morgan, Director of the Office of Resource Development.

The committee met jointly with the Assembly Committee on Membership Recruitment and Participation on Friday, Nov. 9, 1990.

Certain information contained in this report has been updated since the November meeting.

INFORMATION ITEMS

Membership Development

The total membership as of April 1, 1991, was 36,997, which represents a 1.8% increase since April 1, 1990, when the membership total was 36,348. Members-in-Training represent 15.6% of the total membership and continue to be the greatest source of General Members. The distribution by member class for the years 1987 to 1991 can be seen in table 1. A 5-year summary of percentage changes in membership by area is presented in table 2. The Committee on Membership commended Area V for its dedication and consistent commitment to uphold APA's membership development goals. Area V has enthusiastically supported the campaign to recruit residents from its very inception, and the steady growth attests to the overall quality of their recruitment/retention efforts. The Area V executive staff has responded effectively to a clear mandate from their officers. A congratulatory letter has been sent to Area V representatives, presidents, and executive staff.

During 1990, 1,226 Members-in-Training were advanced to General Member status as compared to 182 newly enrolled General Members. Table 3, comparing new General Member enrollment with advancement from Member-in-Training for the past 5 years, clearly shows the value of retaining younger members.

Overall, reinstatements and advancements in member status were greater in 1990 than in 1989, whereas enrollment of new members fell slightly. Specific membership transactions during all of 1990 can be seen in table 4, and a summary of transactions from 1981 to 1990 is shown in table 5.

Selected Recruitment Projects

The Committee on Membership received requests from the Committee on Women and the Council on International Affairs to explore the feasibility of recruiting women and international psychiatrists, respectively. Dr. Benedek agreed to participate in the membership drive for women, and a letter was mailed to 1,248 female psychiatrists in January 1991 over her signature and that of Dr. Norris. The committee will request additional information from the Council on International Affairs regarding increasing the scope of membership offered psychiatrists in the international community.

Membership Losses

The committee reviewed the list of members who faced termination of their membership for nonpayment of 1989 APA dues. In

July 1990, 1,358 members were notified by certified letters from APA's Treasurer that their 1989 dues were in arrears; by the end of October 1990, this number had been reduced to 609 members. Lists of names were sent to the district branches for follow-up retention efforts. *Members of the Assembly were strongly encouraged to contact their respective district branches to assist in personal contact with these members to encourage them to retain their APA affiliation.* Table 6 compares total membership with membership terminations, by area and other characteristics.

Subscription Fee for Life Members/Fellows

In September 1990 the Board of Trustees approved a \$40 fee for Life Members/Fellows wishing to subscribe to the *American Journal of Psychiatry*, which is currently provided at no cost to these members but will cease to be a perquisite because of the increasing proportion of members with Life status. The implementation date has been set as July 1, 1991. To alert the affected members of this change, a letter was sent in late November and a follow-up letter was mailed in April 1991. A tear-off card at the bottom of the letter could be returned if the member chose to subscribe.

Requests for Dues Relief

The committee noted a 30% increase in the number of requests for dues relief, from 318 in 1989 to 404 in 1990, although the number of members making this type of request remains small (1.4% of all dues-paying members).

The committee will continue to focus on increased communication with the district branches. This is necessary to ensure commonality of goals and a better understanding of the philosophy of membership retention and the financial impact that dues relief actions have on the economic stability of district branches. It was recognized that offering temporary dues relief to members in need has enhanced membership retention; nevertheless, the committee felt strongly that since there is more knowledge of a member's particular circumstances at the local level, recommendations are needed from the district branch to arrive at an equitable decision. When the district branch finds it necessary to deny a member's request, the committee will request information on the rationale for its action.

Amendment to Constitution and Bylaws Regarding Life Status

The committee discussed the implementation of the proposed amendment to the Constitution and Bylaws affecting Life status and dues. The proposed amendment would affect those who reach Life status in 1993 and thereafter. If it is passed by the membership, these members will pay two-thirds of the highest dues rate during the first 5 years after reaching Life status and one-third of the highest rate for the second 5 years. Thereafter, those who hold Life status will be exempt from paying dues.

Meeting With District Branch Executive Staff

After the joint meeting of the constitutional and Assembly membership committees, members of both committees met with district branch executive staff to clarify areas of concern. Discussion focused on the need for uniform dues waiver guidelines. Concern was expressed over the types of letters that members receive from the Central Office informing them of the option to request dues relief/Inactive status if they experience financial hardship or some other condition prohibiting payment of dues. At the request of a district branch, the Committee on Membership agreed that the letters will be revised so that members will be advised to contact their district branches to ex-

TABLE 1. Members in Each Class, 1987–1991

Membership Class	Jan. 1, 1987		Jan. 1, 1988		Jan. 1, 1989		Jan. 1, 1990		Jan. 1, 1991		April 1, 1991	
	N	%	N	%	N	%	N	%	N	%	N	%
Dues-paying	27,482	82.3	28,091	81.9	28,250	80.4	28,917	79.9	29,263	79.3	29,366	79.4
Member-in-Training	5,054	15.1	5,366	15.6	5,594	15.9	5,856	16.2	5,760	15.6	5,766	15.6
Associate Member	330	1.0	302	0.9	263	0.8	228	0.6	192	0.5	190	0.5
General Member	18,340	54.9	18,653	54.4	18,847	53.6	19,299	53.3	19,791	53.6	19,898	53.8
Fellow	3,758	11.3	3,770	11.0	3,546	10.1	3,534	9.8	3,520	9.5	3,512	9.5
Dues-exempt	5,206	15.6	5,607	16.3	6,260	17.7	6,570	18.2	6,887	18.6	6,835	18.5
Life Member	1,231	3.7	1,365	4.0	1,700	4.8	1,844	5.1	2,007	5.4	1,994	5.4
Life Fellow	2,609	7.8	2,753	8.0	3,033	8.6	3,133	8.7	3,215	8.7	3,186	8.6
Life Associate	34	0.1	39	0.1	52	0.2	55	0.2	63	0.2	63	0.2
Subtotal	3,874	11.6	4,157	12.1	4,785	13.6	5,032	14.0	5,285	14.3	5,243	14.2
Inactive Member	587	1.8	682	2.0	713	2.0	745	2.1	777	2.1	775	2.1
Inactive Fellow	129	0.4	132	0.4	119	0.3	115	0.3	109	0.3	103	0.3
Corresponding Member	334	1.0	350	1.0	362	1.0	393	1.1	425	1.2	428	1.2
Corresponding Fellow	219	0.6	222	0.6	220	0.6	228	0.6	235	0.6	230	0.6
Distinguished Fellow	30	0.1	30	0.1	31	0.1	28	0.1	27	0.1	27	0.1
Honorary Fellow	33	0.1	34	0.1	31	0.1	29	0.1	29	0.1	29	0.1
Subtotal	1,332	4.0	1,450	4.2	1,475	4.1	1,538	4.2	1,602	4.3	1,592	4.3
Subtotal	32,688	98.2	33,698	98.2	34,510	98.1	35,487	98.0	36,150	97.9	36,201	97.8
Medical Student Member	605	1.8	608	1.8	658	1.9	721	2.0	768	2.1	796	2.2
Total	33,293	100.0	34,306	100.0	35,168	100.0	36,208	100.0	36,918	100.0	36,997	100.0

TABLE 2. Percent Change in Membership by Area, 1986–1990

Membership Group	% Increase in Membership				
	1986	1987	1988	1989	1990
Area					
I	6.2	3.5	5.5	4.9	1.8
II	3.2	1.8	0.9	0.1	1.0
III	4.3	4.3	1.4	3.6	2.6
IV	6.4	2.6	2.1	2.5	1.2
V	5.3	5.5	4.7	3.9	4.0
VI	1.8	0.7	2.1	2.9	-0.1
VII	6.8	3.9	2.8	5.8	3.2
Total	4.8	3.2	2.8	3.1	2.0
At-Large					
Members	0.9	-0.5	-2.3	-0.1	0.5
Total	4.6	3.0	2.5	3.0	2.0

plore available options, which *may* include dues relief or reductions. Since the district branches have more direct contact with their own members, responses to requests for resignation/dues relief can best be personalized at the local level.

The criteria for evaluating dues relief were discussed. The committee will develop guidelines that are more specific than those currently listed in the "Operations Manual of the Board of Trustees."

During the orientation for district branch presidents-elect held each November, the committee will conduct a workshop with the presidents-elect to familiarize them with membership and fellowship issues. The Office to Coordinate the Board and Assembly will be contacted in this regard.

Resource Development Committee

Dr. Harvey St. Clair, chairperson of the Resource Development Committee, and Ms. Andrea Morgan, Director of the Office of Resource Development, joined the Committee on Membership and requested its support. The committee fully endorsed the Resource Development Committee's efforts to enhance APA's financial stability and to fund special important projects through voluntary contributions from various sources, including the APA membership.

The Resource Development Committee noted that industry studies show that fund-raising efforts are more successful when home addresses are used for solicitation. The Committee on Membership encouraged the Office of Resource Development to ask APA mem-

TABLE 3. General Members Gained From Enrollment and Advancement, 1986–1990

Year	Total New General Members	Enrolled	Advanced From Member-in-Training	
			N	%
1986	1,107	395	712	64
1987	1,105	285	820	74
1988	1,185	263	922	78
1989	1,285	215	1,070	83
1990	1,408	182	1,226	87

bers for their home addresses. It was noted that the membership file presently contains a "preferred mailing address" and, if requested by the member, a separate billing address; whether the preferred mailing address is a home or office address is not distinguishable. The committee also indicated that because of the particular population psychiatrists serve, it is important to obtain the member's permission for use of a home address because of privacy and personal safety issues.

Fellowship

The Committee on Membership received 249 nominations for Fellowship from 61 district branches, and it recommended to the Board that 187 nominations be approved, 61 nominations be deferred, and one request for a waiver of a requirement be denied. It was noted that the approval rate of 75.4% is lower than the rates in previous years (85.9% in 1989). The committee will continue to stress to district branch fellowship committees the importance of documenting nominees' qualifications; it is essential that letters of support address the candidates' excellence very specifically. To ensure a fair evaluation of the candidate, the screening process at the local level should monitor carefully the quality of the supporting materials, and, if necessary, the district branches are encouraged to request additional or expanded information from those supporting the nomination.

The committee asked the Office of Membership to combine the criteria for election to Fellowship with an explanation of the committee's guidelines used in the review of each category. The revised criteria were mailed to the district branches in February for use in the 1991 Fellowship election process.

As a means of publicizing the Fellowship guidelines and process and

TABLE 4. 1990 Membership Transactions

Transaction ^a	N
Gains	1,907
New members	1,745
Medical Student Members	332
Members-in-Training	1,199
General Members	182
Corresponding Members	24
Corresponding Fellows	5
Distinguished Fellows	1
Honorary Fellows	2
Reinstatements	162
Medical Student Members	1
Members-in-Training	36
General Members	123
Fellows	2
Losses	1,197
Resignations and drops	992
Resignations from APA	303
Drops for nonpayment of APA dues	454
Other APA drops	3
Drops/resignations from district branches and thus from APA	232
Verified deaths	205
Net gain	710
Changes in membership status	2,055
To Member-in-Training from	182
Inactive Member	1
General Member	22
Medical Student Member	159
To General Member from	1,230
Member-in-Training	1,226
Inactive Member	2
Associate Member	2
To Corresponding Member from General Member	12
To Corresponding Fellow from Corresponding Member	2
To Fellow status from	187
General Member	185
Life Member (to Life Fellow)	2
To Life status from	442
Fellow (to Life Fellow)	179
General Member (to Life Member)	186
Life Member/Fellow (to 50-Year Life Member)	70
Associate Member (to Life Associate)	7
Transfers of district branch affiliation	1,160
Between district branches	1,124
From Member-at-Large to a district branch	19
From a district branch to Member-at-Large	17
Recommendations for deferral or denial of Fellowship status ^b	62
Deferral of transfer of General Member to Fellow	61
Denial of waiver of 2-year waiting period for renomination for Fellowship (not reviewed)	1
Requests for dues relief or Inactive status	404
Approved	293
Dues waiver	112
Dues waiver for reinstatement	10
Dues waiver to reach Life status	28
Reduction of dues	61
Refund of dues	1
Extension/deferral of payment	4
Transfer to Temporary Inactive status	7
Transfer to Permanent Inactive status	61
Transfer to Permanent Inactive status with waiver	8
Transfer to General Member retroactively	1
Deferred or denied	111
Temporary Inactive status	2
Permanent Inactive status	5
Dues waiver	25
Dues waiver to reach Life status	4

TABLE 4 (continued)

Transaction ^a	N
Deferred or denied, cont'd	
Reduction of dues	7
Refund of dues	1
No action pending district branch recommendation	67

^aIn addition, 7,012 address changes were processed. This total may be underinclusive since it reflects only one change per member and multiple changes are not reported.

^b249 nominations submitted.

other membership issues, the committee has received Dr. Robert Campbell's agreement that *Psychiatric News* will publish pertinent articles.

Ethics

The committee discussed revocation of Fellowship for members who are suspended, reporting of names of members whose membership is terminated for nonpayment of dues during ethics investigations, and the effect of suspension on credit toward Life status ("95 formula").

These issues had been previously discussed at an earlier meeting of the Committee and had been referred to the Ethics Committee in September 1990 for its opinions. The Committee on Membership reviewed the opinions of the Ethics Committee and planned to continue its discussion on these issues with members of the Ethics Committee during the 1991 annual meeting.

Committee of Young Psychiatrists

Jane Wells, M.D., a member of the Committee of Young Psychiatrists, joined the Committee on Membership to discuss issues of concern to young psychiatrists (defined as those under 40 years or within the first 5 years past residency). Dr. Wells reported that the Committee of Young Psychiatrists is concerned about the perception of some young psychiatrists that the costs of APA membership are greater than the benefits. To obtain more information on membership losses, that committee will be conducting a pilot study in Maryland to monitor young psychiatrists who drop out of the Association.

At the request of the Committee of Young Psychiatrists, the letter routinely sent by the Office of Membership to those who have advanced from Member-in-Training to General Member has been revised to include a paragraph informing new General Members about the existence of the Committee of Young Psychiatrists.

Race/Ethnicity

The Committee on Membership noted that the membership application has blanks for applicants to check off their race/ethnicity. Input was sought from the Council on National Affairs and the Office of Minority/National Affairs to ascertain how the race/ethnicity options were chosen. For example, there are separate blanks for "Puerto Rican," "Mexican/Mexican American," and "Other Spanish Descent." The rationale for having these three options was unclear to the committee. In addition, "American Indian" and the "Black/Afro-American" may no longer be the appropriate designations.

It was noted that "foreign medical graduate" has been replaced with "international medical graduate."

Census of Residents

Detailed statistical information from the 1989–1990 APA census of psychiatry residents was distributed to the committee. A total of 6,072 residents were reported for the 1989–1990 census year. There was a slight increase in the number of physicians undertaking psychiatry residency training (24 more than in the 1988–1989 census year). The number and percentage of female residents continues to increase: there are 467 more female psychiatry residents now than in 1985–1986, compared to an increase of 125 male residents. In September

TABLE 5. Summary of Membership Transactions, 1981–1990

Transaction	Dec. 31, 1981	Dec. 31, 1982	Dec. 31, 1983	Dec. 31, 1984	Dec. 31, 1985	Dec. 31, 1986	Dec. 31, 1987	Dec. 31, 1988	Dec. 31, 1989	Dec. 31, 1990
Gains	1,422	1,527	2,242	2,169	2,037	2,213	1,880	1,838	2,042	1,907
New members	1,344	1,397	2,190	2,076	1,951	2,068	1,732	1,723	1,930	1,745
Reinstatements	78	130	52	93	86	145	148	115	112	162
Losses	764	642	588	661	714	757	867	976	1,002	1,197
Resignations	152	101	105	133	151	163	211	235	211	303
APA drops	299	266	226	312	249	281	336	328	412	457
District branch drops	92	38	34	61	77	101	136	87	164	232
Deaths	221	237	223	155	237	212	184	326	215	205
Net gain	658	885	1,654	1,508	1,323	1,456	1,013	862	1,040	710

TABLE 6. 1990 Membership Terminations for Nonpayment of 1989 Dues

Group	Total Members	% of Member- ship	Members on Drop List	% of Drop List
Area	36,918	100.0	442	100.0
I	4,263	11.6	46	10.4
II	5,395	14.6	81	18.3
III	5,042	13.7	39	8.8
IV	6,427	17.4	102	23.1
V	7,282	19.7	95	21.5
VI	3,977	10.8	28	6.3
VII	2,810	7.6	46	10.4
Members-at-Large	1,722	4.7	5	1.1
Sex				
Male	27,731	75.1	306	69.2
Female	9,046	24.6	132	29.9
Unknown	141	0.4	4	0.9
Location of medical school				
United States or Canada	27,070	73.3	264	59.7
Other	7,949	21.5	126	28.5
Unknown	1,899	5.1	52	11.8
Member class				
Medical Student Member	768	2.1	53	12.0
Member-in-Training	5,760	15.6	124	28.1
Associate Member	192	0.5	6	1.4
General Member	19,791	53.6	256	57.9
Fellow	3,520	9.5	3	0.7

1990, the data were sent to all directors of psychiatry residency training programs and chairpersons of psychiatry departments, along with forms to collect data for the 1990–1991 census.

Reduction in Dues for Psychiatrists Employed in State Hospitals or Performing Community Service in Underprivileged Areas

The committee reviewed correspondence from the Texas Society of Psychiatric Physicians concerning the difficulty in recruiting psychiatrists employed in state hospitals because of the level of APA and district branch dues. In addition, a member who is performing community service in underprivileged areas of the country asked if a special dues category could be considered for members working under these circumstances.

The committee has previously reviewed proposals for creating special dues categories for part-time practitioners, physicians who belong to multiple professional organizations (such as those who also belong to child and adolescent psychiatry societies), and those in public service and on university faculties. In addition to the implementation of a seven-step dues structure, designed to reduce the burden on those establishing their practices, the committee felt that dues relief, in the form of dues waivers or reductions, has been an effective mechanism for accommodating special individual needs. There was committee consensus that special dues categories for these two sets of circumstances were not warranted.

ACTION ITEMS—GENERAL

Lump Sum Dues Payment

The report of the Ad Hoc Committee on Membership and Fiscal Policy, approved by the Assembly in May 1990, included the recommendation that members be given the option of paying dues in a lump sum, i.e., a member could pay a fixed amount and pay no more APA dues for the rest of his or her life. In considering the report of the ad hoc committee, the APA Board of Trustees referred this proposal to the Committee on Membership and the Budget Committee. The Budget Committee requested a legal opinion on the deductibility of the lump sum payment on a member's tax return and considered the issue at its April 1991 meeting.

The Committee on Membership recommended that APA offer a lump sum dues option, and the Budget Committee concurred. With the current maximum dues (\$460), the lump sum rates would be as follows (through Dec. 31, 1991): age 40–44—\$9,000; age 45–49—\$8,250; age 50–54—\$7,500; age 55–59—\$6,500; age 60–64—\$5,000; age 65–69—\$3,500. The lump sum amounts would be revised annually to reflect changes in the highest annual dues. The amounts for Canadian members would be approximately 40% less, in keeping with the dues reduction they receive.

Under the current rules of the U.S. Internal Revenue Service, for purposes of calculating federal tax, a significant percentage of this payment is deductible from the member's income as a charitable expense in the year in which the payment is made.

It was therefore recommended that the following procedures be implemented to create the lump sum dues option.

1. APA shall establish a program whereby a General Member or Fellow who is 40 or more years of age may pay a lump sum to the Association and shall not be required to pay further annual dues. To continue as a General Member or Fellow of APA, such a member must continue to meet all other requirements of membership, including ethical conduct, continuing medical education, and good standing in a district branch of the Association.

2. Such a member will receive APA publications until he or she reaches dues-exempt status. At that time, the member will be subject to any subscription fee then applicable to dues-exempt members for continued receipt of APA publications.

3. There will be no refund of the lump sum dues payment to the member or his or her estate for any reason, including untimely death, disability, resignation, or expulsion from the Association.

4. The APA Treasurer shall establish a special fund, to be called the Continuing Dues Payment Fund. A portion of each lump sum dues payment shall be deposited in this fund, in an amount to be determined by financial staff. An amount equal to the annual dues the member would have paid will be paid from this fund into the membership dues account each year.

5. The APA Treasurer shall create a special fund, to be called the Board Restricted Investment Fund, for the receipt and investment of all proceeds from lump sum dues not deposited in the Continuing Dues Payment Fund. Ordinary income from this fund will be considered operating income by APA each year. The principal of the fund may not be expended without special authorization of the Board of Trustees.

6. APA shall allow payment of the lump sum in two installments over 2 years or less, provided that the member pays an installment fee equal to 10% of the second payment.

7. The staff and the Budget Committee shall report to the membership in May 1992 on the implementation of the lump sum dues payment program, the number of members who have exercised the lump sum dues option, and the amounts invested in the Continuing Dues Payment Fund and Board Restricted Investment Fund from lump sum dues payments.

During its November 1990 meeting the Assembly approved the recommendation of the committee, and in 1991 the Board of Trustees, with the concurrence of the Budget Committee, approved the recommendation and authorized beginning the option of lump sum dues payments in the fall of 1991.

Dues Amnesty for Former Members

In December 1988, on the recommendation of the Committee on Membership, the Board of Trustees approved a one-time amnesty for former members owing dues before 1988 who wished to rejoin during 1990. The amnesty forgave APA and district branch dues in excess of 1 year's debt, and reinstated members were required to pay the earlier dues owed at the time of membership termination. During 1990, there were 44% more reinstatements of General Members and Fellows than in 1989 (125 reinstatements in 1990 versus 87 in 1989).

To further encourage membership growth and because the recruitment of former members was delayed until May 1990, the committee recommended extending the amnesty period through 1991. The amnesty policy is exactly as it was during 1990, that is, forgiveness of 1 year's dues owed before 1988. In December 1990 the Board of Trustees approved the committee's recommendation that the amnesty be continued through 1991 and that the amnesty apply only to those who owe dues for years before 1988.

Medical Student Members

In March the membership passed an amendment to the Constitution and Bylaws that exempts medical students from district branch membership and requires them to pay a one-time fee, rather than yearly dues. The committee earlier expressed its interest in keeping the fee low and recommended a one-time fee of \$25. Also, approval of the amendment necessitated shifting the responsibility for acceptance of medical students for membership to someone other than the district branch staff/officers. The committee recommended that the "Operations Manual of the Board of Trustees" state that acceptance of Medical Student Members into APA be handled administratively by the Office of Membership, in consultation with the Committee on Membership as appropriate. In December 1990 the Board of Trustees approved a \$25 one-time fee for medical students and acceptance of Medical Student Members by the Office of Membership.

Implementation of Seven-Step Dues Structure

On the recommendation of the Ad Hoc Committee on Membership and Fiscal Policies, the Board of Trustees voted in June 1990 to replace the current three-step phase-in of General Member/Fellow/Associate Member dues with a revenue-neutral seven-step dues structure leading to the highest rate in the eighth year. The Committee on Membership and the Committee of Young Psychiatrists stated their belief that such a dues structure will reduce the financial burden on members just establishing their practices and recommended that the new structure begin with the 1992 dues year. This recommendation was approved by the Board of Trustees in December 1990.

ACTION ITEMS—MEMBERSHIP PROCESSING

Failure to Advance

The committee reviewed correspondence concerning a member of the Bronx District Branch who had maintained Member-in-Training status for 16 years and had not complied with advancement policies. The branch had taken no action to terminate the member's membership for

failure to upgrade, so the committee recommended dropping the individual from APA and district branch membership for failure to advance.

Dual Membership Requirement

The committee reviewed two requests to maintain membership in APA but not a district branch. The committee recommended denial of these requests and continues to uphold the importance of dual membership.

Requests for Review of General Membership Eligibility

Two applications for General Membership, submitted by the Quebec and Eastern Canada District Branch and the Oklahoma Psychiatric Society, were reviewed by the committee. On the basis of the information in the applications, it appeared that neither applicant met the basic eligibility requirement of completion of a residency program in psychiatry accredited by the Residency Review Committee for Psychiatry of the Accreditation Council for Graduate Medical Education or the Royal College of Physicians and Surgeons of Canada. The committee, therefore, recommended that both applications for membership be denied.

Applications for Associate Membership

The committee recommended denial of three applications for Associate Membership submitted by the Northern California Psychiatric Society, the Quebec and Eastern Canada District Branch, and the Western New York Psychiatric Society. The denial was based on the committee's recommendation that this category of membership be abolished and the Board's 1989 decision that, pending Constitutional changes, no new applicants for this category will be accepted.

Request to Maintain Medical Student Membership

The committee recommended denial of a request from a Medical Student Member for permission to remain an APA member until July 1991, when the member expected to be enrolled in a psychiatry residency program. The committee recommended denial of the request because the member would not meet the requirements for membership as either a Medical Student Member (enrollment in medical school) or a Member-in-Training (acceptance into an approved psychiatry residency program). The physician will be encouraged to re-apply when eligible and to maintain ties with APA through subscriptions to the *American Journal of Psychiatry* and *Psychiatric News*.

Fellowship Nominations

The committee received 249 nominations for Fellowship and reviewed 248; one request for a waiver of the 2-year waiting period for resubmission was denied. Of the 248 nominations reviewed, 187 (75.4%) were recommended for approval by the Board of Trustees. The approval rates in 1989 and 1988 were 85.9% and 87.1%, respectively. The committee recommended that 185 nominations for advancement from General Member to Fellow be approved, two nominations for advancement from Life Member to Life Fellow be approved, and 61 nominations for advancement from General Member to Fellow be deferred.

Nominations for Honorary and Distinguished Fellowship

In accordance with the operations manual, the Committee on Membership acts on nominations by voting members of APA for Honorary Fellow and Distinguished Fellow and forwards its recommendations to the Board of Trustees.

A letter nominating Norman Sartorius, M.D., for Distinguished Fellowship was received from a Life Fellow of APA. The committee reviewed additional letters of support and recommended approval of Dr. Sartorius for Distinguished Fellowship.

Letters nominating Ellen Frank, Ph.D., and Myrna Weissman, Ph.D., for Honorary Fellowship were received from Fellows of APA. The committee reviewed additional letters of support and recommended approval of Dr. Frank and Dr. Weissman for Honorary Fellowship.

TABLE 7. 1990 Resignations by Member Class

Member Class	Resignations	% of Resignations	Members ^a	% of Membership
Medical Student				
Member	44	14.5	768	2.1
Member-in-Training	48	15.8	5,760	15.6
Associate Member	6	2.0	192	0.5
General Member	192	63.4	19,791	53.6
Fellow	9	3.0	3,520	9.5
Life Fellow	4	1.3	3,215	8.7
Total	303	100.0	36,918	100.0

^aAs of Dec. 31, 1990.*Corresponding Members/Fellows and Members-at-Large*

The committee reviewed applications for membership/advancement and recommended that 24 applications for Corresponding Membership be accepted, five nominations for new Corresponding Fellows be accepted, two nominations for advancement from Corresponding Member to Corresponding Fellow be approved, four nominations for advancement from Corresponding Member to Corresponding Fellow be deferred, and one application for General Member-at-Large be approved.

APA Dues Arrearages and Membership Termination

In April 1990, 1,595 letters over the signature of the APA Treasurer were mailed to members whose dues were in arrears for 1989. In July 1990, 1,358 certified letters over the signature of the APA Treasurer were mailed to those who had not responded to the earlier mailing. Extensive retention efforts were conducted in the ensuing months, thereby minimizing membership losses; special emphasis was placed on increased personalized communication with members and district branches. At the end of 1990, the committee recommended and the Board approved dropping the members whose dues were in arrears for 1989, and it was further recommended that administrative reinstatement be authorized for those who returned to good standing by Jan. 31, 1991, and were also in good standing in their district branches. As of the end of 1990, 466 members were notified that their membership had been terminated and were given the 1-month grace period to pay their dues and be administratively reinstated; 24 members did respond during the grace period.

In 1988, in response to a request from the Southern California Psychiatric Society, the Board of Trustees approved the recommendation of the Committee on Membership that, beginning with the 1990 dues year, the schedule for termination of membership for nonpayment of dues be accelerated by 6 months. Consequently, the termination process for members who failed to pay 1990 APA dues began in November 1990, rather than April 1991, as would have been the case before this action. As a result of the change, 3,175 members were notified by letter from the APA Treasurer in November, and the 1,874 who had not responded received a follow-up letter from the Medical Director in January 1991. The 1,569 members who still owed 1990 dues in April 1991 received a certified letter from the APA Treasurer. The effects of the accelerated termination will not be known until June 1991, when membership is terminated for the first group (members whose 1990 dues are in arrears) under the new policy. It is anticipated that membership losses will increase, but every effort is being made to minimize these losses.

Resignations

The committee reviewed the list of names of members who resigned. Under standing authorization of the Board of Trustees, the

TABLE 8. Requests for Dues Relief, 1986–1990

Year	Dues Relief Requests	% of Requests Approved	Dues-Paying Members	% of Dues-Paying Members Requesting Relief
1986	260	84.2	26,451	1.5
1987	321	89.1	27,482	1.2
1988	316	83.5	28,091	1.1
1989	318	83.3	28,250	1.1
1990	404	72.5	28,917	1.4

Medical Director regretfully accepted the resignations. Table 7 shows by member class all 1990 resignations as a percentage of total resignations and as a percentage of members in the class.

Dropping of Members Dropped by District Branches

Chapter Eight of the Bylaws states, "Resignation or loss of membership in the Association or the member's District Branch for any reason shall entail loss of membership in both." The names of members who had resigned from or been dropped by their district branches were reviewed by the committee. The members were advised that loss of branch membership would involve loss of APA membership. The committee recommended that the Board of Trustees authorize dropping from APA membership as of December 1990 members who had resigned from or were dropped by their district branches and further, that the Board of Trustees authorize administrative reinstatement of those who returned to good standing in their district branches and APA.

Dropping of Member for Failure to Hold Valid Medical License

Chapter One of the Bylaws states, "General Members shall be physicians who have completed acceptable training and who hold either a valid license to practice medicine or hold an academic, research, or governmental position that does not require licensure." The committee recommended that a member who was found not to hold a license be dropped from membership in APA and consequently the district branch.

Dues Relief/Inactive Status

Table 8 contains the numbers of dues relief requests from 1986 through 1990. Between those years there was a 55% increase in the total number of requests received. It was noted that there was a substantial increase in the number of dues-paying members who requested relief in 1990 and a marked decrease in the percentage of requests that were approved.

At its November meeting, the committee reviewed 233 requests for dues relief and/or transfer to Inactive status and recommended that 65 waivers of APA dues be approved, 12 waivers of APA dues to reach Life status be approved, two waivers of APA dues to reinstate membership be approved, 18 waivers of APA dues be denied, three waivers of APA dues to reach Life status be denied, 30 requests for dues reductions be approved, two requests for dues reductions be denied, 14 requests for transfer to Inactive status be approved, two requests for transfer to Inactive status be denied, one request for Temporary Inactive status be approved, one request for Temporary Inactive status be denied, one request for a dues refund be approved, three requests for payment plans be approved, one request to defer payment of 1989 and 1990 dues be approved, one request to transfer to General Membership retroactively be approved, and 67 requests for dues relief or Inactive status be deferred pending district branch recommendations. The Board of Trustees approved all of the committee's recommendations regarding membership processing in December 1990.

Report of the Committee of Tellers

Edward C. Kirby, Jr., M.D., Chairperson

The Committee of Tellers met on April 4, 1991, at APA headquarters to certify the results of the 1991 election. Ballots were mailed on Feb. 20, 1991, to 34,285 eligible voting members. From that number 132 undeliverable ballots were deducted. The adjusted number of eligible voting members was 34,153, and 13,571 ballots were returned and included in the final tally (39.7% of the eligible voting members).

The Committee of Tellers acted on uncertain votes that had been held for its decisions. The committee also confirmed that all candidates had verified the accuracy of their biographical statements and had submitted the required statements of compliance with election guidelines.

The Committee of Tellers certified that the following individuals were elected to office and so reported to the Board of Trustees—President-Elect: Joseph T. English, M.D. (58.0% of the votes cast); Vice-President: Leah J. Dickstein, M.D. (52.1%); Secretary: Steven S. Sharfstein, M.D. (51.1%); Trustee-at-Large: Rodrigo A. Munoz, M.D. (51.4%); Member-in-Training Trustee-Elect: Andrea S. Moskowitz, M.D. (52.5%); Area I Trustee: Herbert S. Sacks, M.D. (61.9%); Area IV Trustee: Robert J. McDevitt, M.D. (57.5%); Area VII Trustee: Merlin H. Johnson, M.D. (54.4%).

To have a valid election on changes to the Constitution and Bylaws, 33 1/3% of the eligible voting members must cast votes. Abstain and invalid votes are considered to be votes cast and count toward deter-

mining if 33 1/3% has been reached. Abstain and invalid votes do not count in determining whether a change passes or fails. Once 33 1/3% has been reached, a majority must approve amendments to the Constitution and Bylaws. The results of the vote on the amendments were as follows:

Amendment 1, Chapters 1.4b and 1.5. Votes were cast by 37.1% of the eligible voters. The amendment passed; 91.0% of the votes were in favor. The change abolishes the category of Associate Membership.

Amendment 2, Chapter 1.12. Votes were cast by 37.1% of the eligible voters. The amendment passed; 93.8% of the votes were in favor of the amendment. The change extends the option of Corresponding Membership to members permanently residing in Mexico, Central America, and the Caribbean.

Amendment 3, Chapters 1.4a, 2.1, 2.2, and 8.6. Votes were cast by 36.8% of the eligible voters. The amendment passed; 94.8% of the votes were in favor. The change exempts medical students from the dual membership requirement and yearly dues, requiring only a one-time fee when the medical student joins.

The Committee of Tellers recommended that the Board of Trustees accept the results of the 1991 election, and the Board accepted them. The Board also approved a recommendation by the Committee of Tellers to dispose of the ballots from the 1991 election after the 1991 annual meeting.

Subspecialization in Psychiatry

The knowledge and database of psychiatry have expanded enormously. As a reflection of this abundance, subspecialization has come to psychiatry. Previously, the only official subspecialty was child psychiatry. In 1989, geriatric psychiatry was approved by the American Board of Medical Specialties as an area of added qualification for psychiatrists, and currently addiction psychiatry is under review by the same body (1). The APA Commission on Subspecialization, the Assembly, and the Board of Trustees have recommended that forensic psychiatry be granted the status of subspecialization.

The subspecialty movement has been viewed ambivalently by many because of concerns about fragmenting our field, restricting practices of those who do not have certificates of subspecialization, and the potential for ignoring the teaching of these subspecialty areas to general psychiatry residents. Both pediatrics and internal medicine have faced this problem much earlier than psychiatry, and while the advent of subspecialization in these disciplines has led to some fragmentation, the overall strengthening of these fields has been impressive.

The American Board of Psychiatry and Neurology (ABPN) formally began examining the questions of subspecialization at a meeting in 1986. At that time, the Board set up criteria for the process of defining subspecialty areas. These were based in part on criteria developed by the American Board of Internal Medicine, which noted the following:

1. The existence of a separately and specifically identifiable scholarly discipline with a significant scientific base and a clear-cut relationship to psychiatry;
2. The recognition of this discipline in the medical, academic, and scientific communities;
3. The potential for a critical mass of physicians in well-defined practice in this area;
4. The existence of formal training programs with prescribed standards;
5. The creation of this new subspecialty area should lead to improved care and be in the public interest.

It was also felt at that time that these decisions must come at the urging of the whole field of psychiatry and not primarily from individual groups or subgroups of physicians, but through a defined process within APA. Through the fulfillment of these criteria and through the mechanisms prescribed by APA, this has led to the current subspecialty and pending designations.

However, other ways of achieving subspecialty status for psychiatrists are emerging, particularly in areas where the discipline cuts across specialty lines such as pain management, and specifically in clinical neurophysiology. Primarily at the urging of the general field of neurology, the ABPN proposed the issuing of new certificates of added qualification in clinical neurophysiology. In September 1990, the American Board of Medical Specialties approved this. While the majority of clinical neurophysiologists are neurologists, there are many psychiatrists who do electroencephalographic and evoked potentials studies for diagnostic purposes. These psychiatrists

feared that they might be excluded from this area. Recognizing this, the Board voted to allow any certified psychiatrist who does a significant amount of clinical neurophysiology to sit for this examination until 1997.

Beginning in 1997, those diplomates of the ABPN with unlimited licenses to practice medicine who wish to receive certification in clinical neurophysiology will be required to satisfactorily complete 1 additional year of training in clinical neurophysiology. These programs, which will be open to graduates of psychiatry residencies as well as neurology residencies, must be approved by the Neurology Residency Review Committee of the Accreditation Council of Graduate Medical Education. In addition to the training requirement, those wishing certification must pass a multiple-choice examination. Between now and 1997, the required year of training can be replaced by 3 years or its equivalent of practice in the subspecialty.

Clinical neurophysiology is the application of electrophysiology to the assessment of CNS disorders and includes electroencephalography, electromyography, nerve conduction studies, and evoked potentials for diagnostic or monitoring purposes.

Psychiatrists may receive teaching and experience in these areas during residency. After this training, psychiatrists can and do elect to apply one or more of these studies in their practice on the basis of their own evaluation of their capability. Some psychiatrists have elected to take additional training and experience in these areas. Such additional training varies in three major ways.

1. The amount of additional time varies from a few months to 2 years.
2. The additional training may include one or more subsets of the field of clinical neurophysiology, such as electroencephalography alone, electroencephalography and evoked potentials, or electroencephalography and other combinations.
3. The type and depth of additional study by each individual in each area vary and may include any combination of clinical practice skills, educational experience, and research depending on the interest and goals of the psychiatrist.

Added qualification in clinical neurophysiology was, therefore, defined as the only mechanism through which diplomates of the ABPN could receive recognition for subspecialization in either electroencephalography or electroencephalography/evoked potentials. It was agreed that such certification would be accomplished with as little disturbance of the excellent current programs and experience as possible.

Training programs in clinical neurophysiology must be 1 year in length but allow flexibility in how the time is spent, just as in psychiatry residency programs. Individual trainees can focus on one area such as electroencephalography or spend time in a combination of areas of study. Trainees can spend time in elective areas that are related to clinical neurophysiology, just as they spend time in nonpsychiatry areas during residency.

The training program is responsible for providing the specific skills required for the areas learned and administers tests to ensure technical competence. The assurance of acquisition of these skills is the responsibility of the director of the training program.

The second major element of certification of added qualification is formal testing of cognitive knowledge by the ABPN. The test is designed to recognize the variety of training and clinical experiences of the candidates. While there will be questions on each of these areas of knowledge in clinical neurophysiology, including electroencephalography and electromyography, a large proportion of the examination will test those areas of basic knowledge required of individuals working in each of these areas such as physiology, neuroanatomy, wave form analysis and quantitation, averaging, stimulation, and recording and instrumentation. The construction of the examination is, therefore, comparable to what is necessary when writing broader-based examinations such as those for radiology, which must cover diagnostic CT scanning, nuclear scanning, ultrasound and magnetic resonance imaging (2).

The first certification examination for added qualification in clinical neurophysiology will be administered at six locations on March 31, 1991. The second examination has not yet been scheduled. It is anticipated that the application deadline will be September 1 before an April examination. It is anticipated that the second examination will be administered no later than April 1993. Inquiries should be sent to the American Board of Psychiatry and Neurology, Suite 335, 500 Lake Cook Rd., Deerfield, IL 60015.

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Psychotherapist-Patient Sexual Contact After Termination of Treatment: An Analysis and a Proposal

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Controversy over the legitimate extent, if any, of sexual contact between psychotherapists and former patients remains intense. In this paper the authors review current approaches to controlling posttermination sexual contact, offer a conceptual framework within which the problematic aspects of therapist-patient sex both during and after treatment can be understood, and develop a set of recommendations for policies that balance the goals of protecting former patients and avoiding unnecessary interventions into consensual relationships. Review of ethical, legal, and administrative controls on posttermination sex revealed considerable heterogeneity of approaches, which appeared to be based on confusion concerning the rationale for restriction. An analysis of the problems with therapist-patient sexual contact suggests four areas of concern: impaired decision making, coercion, fraud, and exploitation of a fiduciary relationship. The nature and magnitude of these problems differ in pre- and posttermination sexual relationships. The authors conclude that clarity of restrictions on posttreatment sex is important, but an absolute ban is not essential to protecting former patients. Rather, a 1-year waiting period after termination, during which even social contact would be precluded, should minimize problems and allow former patients and therapists to enter into intimate relationships. The authors discuss the advantages and disadvantages of this approach over other approaches.

(Am J Psychiatry 1991; 148:1466-1473)

All major mental health organizations condemn psychotherapists' sexual contact with patients in treatment (1-4). However, debate still rages over the ethics of posttermination psychotherapist-patient sexual contact. In a national survey of psychiatrists (5), approximately one-third of those responding thought that sex with a former patient might be appropriate. Two studies of psychologists (6, 7) reflected the same split between those who thought posttermination sex might be acceptable and those who thought it unethical.

One study of psychotherapists on the faculty of the department of psychiatry of a major medical school (8) found that only 29.6% believed that marrying a patient after proper termination of long-term therapy was unethical.

Given this diversity of opinion, it is not surprising that the major medical and mental health organizations have been unable to agree on how to deal with posttermination sexual contact. In 1988, the American Psychiatric Association amended its ethics code to read, "Sexual involvement with one's former patient generally exploits emotions deriving from treatment and therefore almost always is unethical" (1). Two years later, the American Medical Association branded as unethical only relationships in which the physician "uses or exploits trust, knowledge, emotions, or influence derived from the previous professional relationship" (9). In contrast, the American Association for Marriage and

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Family Therapy amended its ethics code in 1988 to prohibit sexual contact with former patients only for 2 years after termination (10). Other mental health organizations continue to consider the issue (11, 12); the American Psychological Association recently proposed a draft standard that would require the psychologist to demonstrate that a relationship was not exploitative, and an optional section would add a flat ban on sexual contacts for 1 year after termination (13).

As with the general problem of psychotherapist-patient sex, however, the initiative for dealing with posttermination sexual contact is being taken out of the hands of the mental health professions (14). Given what is generally perceived as the professions' failure to respond adequately to the phenomenon, courts are beginning to establish their own common law approaches to cases involving psychotherapists' sexual contact with former patients, and legislatures are moving to enact statutory penalties, both civil and criminal. Administrative bodies, such as boards of licensure, also are imposing sanctions more frequently for posttermination sexual contact.

These rapidly developing regulatory efforts are marked by the same diversity of approaches that characterizes mental health professionals' reactions to the problem. Even more troublesome, the rules that have been formulated are frequently unclear, leaving patients, therapists, and regulators uncertain as to whether the behavior they are about to initiate or sanction has violated the applicable standards. We believe that a large part of the difficulty stems from a lack of conceptual clarity about why psychotherapist-patient sexual contact after termination is undesirable. Without a sound theoretical basis, regulatory responses have a random quality.

In this paper we review current approaches to controlling posttermination sexual contact. We then offer a conceptual framework within which the problematic aspects of therapist-patient sex, both during treatment and after termination, can be understood. We believe this approach unifies, in a manner consistent with established law, the major reasons offered for rejecting sexual contact with former patients. From this understanding, we develop a set of recommendations for reasonable policies that achieve the goal of protecting former patients while avoiding unnecessarily paternalistic interventions in consensual relationships.

CURRENT APPROACHES

Criminal Law

Legislation criminalizing posttermination sexual contact illustrates the diversity of current approaches to the problem. Statutes making psychotherapist-patient sexual contact a crime have been passed in seven states—California (15), Colorado (16), Florida (17), Maine (18), Minnesota (19), North Dakota (20), and Wisconsin (21). Only three of the states—California, Florida,

and Minnesota—have addressed posttermination sexual contact. Both California and Florida criminalize sexual contact with former patients if the therapist terminates the therapeutic relationship primarily for the purpose of engaging in sexual acts with the patient. In California, however, a therapist may avoid criminal liability even if the relationship is terminated primarily for sex, if the therapist refers the patient to "an independent and objective psychotherapist, recommended by a third-party psychotherapist." The statute appears not to require that the consultation actually take place, as long as the referral is made.

Minnesota provides much more stringent restrictions. Criminal penalties apply if the therapist has sexual contact with a former patient who is "emotionally dependent" on the psychotherapist or if there has been any "therapeutic deception" of the patient. (Therapeutic deception is defined as a claim by the therapist that sexual contact is "consistent with or part of the patient's treatment.") The statute does not limit the period of time covered. Thus, if a patient is emotionally dependent on the therapist even 10 years after the termination of therapy, a criminal complaint may still be made. However, the only case brought under this statute to date failed, as the patient's emotional dependence on the therapist could not be proved beyond a reasonable doubt (22).

Criminalization represents one end of the spectrum of possible sanctions for sexual contact between former patients and psychotherapists. Adoption of criminal statutes has been inhibited by concern that it may not be possible to formulate the elements of the offense clearly enough to pass constitutional muster, e.g., to determine whether the patient is still under the influence of a positive transference (23). As a result, four of the seven states that criminalize sexual contact with current patients have opted to avoid criminal sanctions for posttermination sexual contact. A legislatively authorized committee in Massachusetts, one of the states now considering criminal measures for sexual contact with current patients, has also chosen not to include a provision for former patients (24). Members of the group believed that civil law and administrative boards are better suited for regulation of posttermination sexual relationships.

Civil Statutes

While most civil actions are brought under common law, four states have passed statutes providing a civil cause of action for sexual exploitation of patients by their psychotherapists, whether licensed or unlicensed. All four states—California (25), Illinois (26), Minnesota (27), and Wisconsin (28)—cover posttermination sexual contact between therapist and patient. California and Minnesota prohibit sexual contact with a former patient for 2 years. California makes this an absolute prohibition, whereas Minnesota requires, as it does under its criminal statute, that the patient prove emotional dependence on the psychotherapist at the time of

the sexual contact or that the sexual contact resulted from therapeutic deception. Illinois has a statute identical to that of Minnesota except the prohibition extends for only 1 year.

The most far-reaching statute is that of Wisconsin. Wisconsin covers any person who suffers an injury as a result of sexual contact with a therapist who is rendering or has rendered psychotherapy to that person. This covers former patients if harm can be shown. In effect, this statute adopts the rule that, if harm occurs, posttermination sexual relations between a therapist and patient are never acceptable. Thus, prospective determination of the legal status of a relationship between a therapist and former patient is impossible.

Common Law

Most psychotherapist-patient sex cases in which the patient seeks compensation through the courts are brought as malpractice actions, alleging the negligent treatment of a patient (e.g., 29, 30), although actions for negligent infliction of emotional distress (31), intentional infliction of emotional distress (32), and breach of contract (33) have also been successful. Compared with the large number of cases involving claims against therapists for sexual contact with current patients, few appellate cases involving posttermination sex have been reported. In *Noto v. St. Vincent's Hospital and Medical Center of New York* (34), one of the more egregious cases, the court held that the patient had a valid cause of action against a psychiatric resident for a sexual relationship that began after the termination of therapy. The plaintiff had sought inpatient treatment for drug and alcohol dependency and "seductive behavior." After her discharge, the resident who had treated her smoked marijuana and drank alcohol with her and commenced a sexual relationship that resulted in a pregnancy. The court found that the resident's actions constituted malpractice and intentional infliction of emotional distress. Even though the therapy time was brief, the court particularly noted that the doctor's actions were intended to exploit the plaintiff's specific vulnerabilities.

It appears that the courts, at least in some cases, are willing to construe posttermination sexual contact as a negligent act by the psychotherapist that violates an ongoing duty to the former patient. The extent of acceptable contact with a former patient under the common law, however, remains to be determined. *Noto* suggests that egregious exploitation of the patient's illness is particularly likely to result in liability. The same may be true when actions by the therapist during the course of therapy set the stage for posttermination sex (35).

Administrative Board Regulations

Administrative boards have grants of power from the state legislature to perform various functions, such as licensing and regulating professions. Boards regulating the same professions may have different regulations in

different states, and boards overseeing different professions may have different regulations even in the same state. In Florida, the difference between regulations for psychologists and psychiatrists is especially acute. The Board of Psychology provides that "for purposes of determining the existence of sexual misconduct . . . the psychologist-client relationship is deemed to continue *in perpetuity*" (emphasis added) (36). However, psychiatrists in Florida are bound by the regulations of the medical board, which allows sexual contact between psychiatrist and patient *immediately after termination* (37).

A board may either set standards for a profession or leave decisions to be handled on a case-by-case basis. A recent decision by the Massachusetts Board of Registration in Medicine (38) illustrates some of the problems that may arise if a board decides to avoid setting standards. The case involved disciplinary actions against a psychiatrist for posttermination sexual contact. The patient had entered "focused therapy" with the psychiatrist concerning her mother's illness. When her mother died, the patient terminated therapy and began repeatedly phoning the psychiatrist, requesting a personal relationship. Approximately 2 months after the termination of therapy, the psychiatrist met with the patient, put his arm around her, and kissed her but told her that he could not have sex with her. For 3 more months, the psychiatrist met with the patient; the sexual contact went no further than kisses and, on one occasion, a back massage given by the patient to the psychiatrist.

The patient reported this activity to a subsequent therapist and, within 2 weeks of the patient's reporting, the psychiatrist's employment was terminated, even though there were no other allegations of substandard care rendered to any other patients. At the board's hearing, the psychiatrist was found to be "guilty of misconduct within the practice of medicine" and "guilty of conduct which undermines confidence in the integrity of the medical profession and for conduct which shows lack of good moral character." The board sanction included a reprimand, a \$5,000 fine, required coursework on transference, and mandatory personal psychotherapy.

The psychiatrist argued in his own defense that he had researched what his ethical role was in relation to a former patient and claimed to have read that "a limited social relationship with a former patient would fall within ethical standards." The board's ethical standards were not clearly set forth, yet the cost of violating them was the loss of the psychiatrist's job and the imposition of disciplinary sanctions.

Professional Societies

Professional societies or associations, such as the American Psychiatric Association or the American Psychological Association, are voluntary groupings of people. Membership is not compulsory, and the governing board has limited power over the members. However, professional societies issue codes of ethics that bind their members and may be highly influential in the de-

cisions of other bodies, such as administrative boards. To date, only the American Psychiatric Association (1), the American Medical Association (9), and the American Association for Marriage and Family Therapy (10) have included guidelines for sexual contact with former patients.

In one case brought before the ethics committee of the American Psychiatric Association (39), a psychiatrist who had had sexual contact with a former patient was expelled from the organization. The reviewing committee's decision stated that "the psychiatrist's sexual involvement with the patient constituted exploitation of the 'knowledge, power and unique position that [the doctor] held in the patient's mental life.'" The failure of most professional groups to report their ethics actions publicly makes it difficult to ascertain the frequency with which actions are being taken against therapists for sexual contact with former patients or the point at which an ethical transgression is deemed to have occurred.

WHY SEXUAL CONTACT WITH PATIENTS SHOULD BE RESTRICTED

Current regulatory efforts aimed at posttermination sexual contact are so diverse as to bespeak a lack of consensus on when sexual contact with former patients should be prohibited. Confusion is apparent over whether sexual contact should be prohibited indefinitely or only for a period of time. Some jurisdictions taking the latter approach set a fixed period of time, while others vary the interval according to the characteristics of a particular case. In some cases, sexual intercourse alone is deemed worthy of sanction, while in others behavior that stops short of actual sexual contact may be prohibited.

What is needed to resolve this divergence of approaches is greater conceptual clarity about the critical question concerning this issue: in a society strongly disposed to allow competent adults to enter freely into consensual relationships (40), why should sexual relationships between psychotherapists and former patients be treated differently? Once it is understood why it may be undesirable to honor the decisions of former patients to enter into such relationships, reasonable and consistent rules regulating the behavior can be constructed. We begin by considering the grounds for the existing consensus that we should not respect the decisions of patients to engage in sexual contact with their current therapists and then ask to what extent the arguments apply to sexual contact after termination of treatment.

Psychotherapist-Patient Sexual Contact

Although it is true that our society generally respects its members' decisions, this is not universally the case. Despite our commitment to individual choice, we do not respect choices made when a person's decision-making capacity is substantially impaired, the person is coerced into making the decision, or the decision is

based on fraudulent representations by one of the interested parties (41). The co-occurrence of two or more of these factors, even if no one of them is by itself sufficiently pronounced to justify disregard of a person's choice, increases the likelihood that we will not respect the decision (42).

These considerations provide a basis for understanding our unwillingness to respect the decisions of patients to engage in sexual contact with their psychotherapists during treatment. A patient who becomes involved in such a relationship (in the vast majority of cases, the patients are women involved with male therapists [43]) is likely to have a significantly impaired ability to decide whether to have sexual contact with the therapist. This impairment may result from two causes: the underlying distress that brought the patient into treatment, which may continue to cloud the patient's judgment, and the transference toward the therapist that develops (44). The latter is often characterized by an idealization of the therapist, including fantasies of gratifying infantile sexual desires, which compromise the patient's ability to weigh the risks and benefits of sexual involvement (45).

Added to these problems with decision making is the presence of a coercive element in the relationship. The patient has arrived in distress, lodging trust and hope in the therapist's ability to relieve pain. The therapist promises to help but instead seeks the patient's sexual favors, either by requesting sexual contact or by responding affirmatively to the patient's sexualization of the relationship. Even when not stated overtly (e.g., "Have sex with me or I will reject you"), there exists an implicit threat that the patient who decides against sexual contact will be abandoned, thereby suffering additional psychic pain and losing what she believes is the prospect of alleviating the underlying condition. Therapists may also have access to information concerning patients' vulnerabilities that makes it easier to pressure patients into sexual activity (44). Commentators on this subject frequently refer to a "power imbalance" between patient and therapist that impairs the patient's ability to choose (5, 46), but it is the manner in which the power is being exercised, not the mere fact of an imbalance, that is the problem.

There is, moreover, often a fraudulent aspect to the therapist's presentation of the possibility of sexual involvement with the patient during treatment. Although reported cases suggest it is becoming less frequent for sexually involved psychotherapists to claim that sexual contact is part of the patient's treatment, another misleading claim is inherent in the situation: "I can still treat you effectively even if you have sex with me." It is difficult to imagine a case in which this would be true, given the conflict in roles between being a lover and a therapist (47, 48). To encourage patients to believe they can gratify sexual desires with their therapists and continue to receive the treatment they need is to deceive them.

Persons who oppose flat bans on therapist-patient sex often argue that the elements just outlined occur regularly in sexual relationships outside the therapeutic set-

ting. People "in love" have notoriously bad judgment about the qualities of their lovers, differentials in power are common and may even be considered erotic, and only a minority of relationships begin without the telling of a few lies (48). Why should psychotherapist-patient sexual relationships be treated differently?

The answer lies in the unfairness of allowing the psychotherapist to benefit from the patient's compromised decision process while the patient risks substantial harm. A therapist enters into a fiduciary relationship with a patient; that is, the therapist assumes a responsibility to act in the patient's best interests, not against them. This duty is inherent in all physician-patient and therapist-patient relations (49). Yet, while the therapist's sexual desires may be gratified, the available data and clinical experience suggest that many women who become involved in sexual relationships with their therapists suffer harm as a result (50).

Taken as a whole, these factors explain why we will not allow patients to agree to engage in sexual contact with their therapists. The quality of their decisions is likely to be affected by their impaired capacity, the coercive aspects of their situation, and fraudulent representations by the therapists. Further, the very persons who are charged with advancing their interests—their therapists—stand to benefit from the situation at their expense. This also explains why, in rejecting a patient's choice to engage in sexual contact, we place the burden on the psychotherapist to ensure that the undesirable conduct does not occur, at risk of civil or criminal liability should the therapist fail to live up to this responsibility.

The one element of our current policies that remains to be justified is the blanket nature of the prohibition of therapist-patient sex. To be sure, not every sexual relationship in therapy will be characterized by the factors discussed. Some patients may make unimpaired decisions, in the absence of coercion, with a clear understanding of the likely consequences, and without subsequent ill effects. As a society, however, we have reached the conclusion that this combination of events is so unlikely and the converse so probable that an absolute ban on psychotherapist-patient sex during treatment is warranted.

Posttermination Sexual Contact

To what extent does this rationale apply after treatment has ended? We believe that there are still reasons for restricting sexual contact but that it is difficult to justify as sweeping a rejection of patients' choices to have sex with their previous therapists. The major factors that lead to an absolute proscription of sexual contact with current patients are all, to a greater or lesser extent, modified in the posttermination context.

Certainly, the decision-making ability of former patients may continue to be impaired, either because of their primary disorders (recall the facts in *Noto*) or residual transference. The magnitude of that impairment, however, is in question. There is a good deal of contro-

versy about the degree to which transference is maintained after termination and the extent to which a "proper" termination attenuates the phenomenon (48). The existing data on this question (see studies cited in reference 39) are fragmentary, methodologically problematic, often based on single case reports, and in several instances susceptible to interpretations supporting both sides of the debate. Moreover, although some data suggest that patients may retain feelings about their therapists for considerable periods of time (51), it is unclear whether these feelings are of the type or magnitude that would interfere with competent decision making. In fact, some studies of postanalysis transference (52, 53) suggest it is used to facilitate reality-based, adaptive responses to new situations. Given the state of the empirical data, we find it reasonable to assume both that some transference continues after the patient leaves the consulting room for the final time (39) and that for most patients the effect diminishes as time passes.

As far as the therapist's potential for coercing the patient into sexual contact is concerned, that should decrease substantially after therapy is over. The implicit threat that treatment will be withheld if the patient refuses sex is now defused. An unscrupulous therapist might threaten to reveal embarrassing information conveyed during therapy, but, according to reported cases, that is uncommon. On the other hand, personal information revealed in the course of therapy might still be used to manipulate the former patient into agreeing to sexual contact (9). The therapist's potential for coercive influence on the patient has diminished but has not disappeared altogether.

Fraudulent characterization of sexual contact as therapeutic also is less likely once treatment has ended. Similarly, the concern that the therapist might mislead the patient into believing sexual relations will not interfere with the therapy loses much of its force. It may be argued that sex which begins after a properly conducted and terminated course of treatment can retroactively undermine the gains that have been achieved (39). To our knowledge, there are no data addressing this question.

Finally, it is more difficult to make an argument for the inherent unfairness of sex between therapist and patient after the therapy has terminated. For most purposes, the fiduciary relationship ends when therapy is concluded. Therapists, for example, are not obligated to resume therapy at the request of former patients (54). Although some residual obligations remain—confidentiality is the best example—as a whole, the fiduciary duties are not of the same magnitude as during therapy. Further, it is uncertain to what extent former patients are likely to be harmed by sexual contact (55). The published literature is devoid of empirical studies on the effects of relationships begun after termination of treatment, and even anecdotal reports are rare.

In sum, the justifications for preventing sexual contact with psychotherapists after termination of treatment are weaker than for pretermination sex. Valid concerns remain, however, with regard to possible impairment of decision making and some aspects of coer-

cion. The question of the degree of harm suffered by former patients involved in sexual relationships remains unanswered. This analysis suggests that, given the general presumption that persons' choices should be respected, there are insufficient grounds to warrant an outright ban on sexual contact after termination of therapy. Rather, more selective interventions are justified to minimize the likelihood that impaired decisions will be made or adverse effects occur.

A PROPOSAL FOR REGULATING PSYCHOTHERAPIST-PATIENT SEXUAL CONTACT AFTER TERMINATION OF TREATMENT

An absolute ban on posttermination sex—now embodied in some statutes (28), argued for by some commentators (5, 12, 39, 55), and approached in the American Psychiatric Association's position (1)—appears to us to be unnecessary, given the nature and magnitude of the problem. Instead, the concerns about allowing patients to enter into sexual relationships with former therapists can be addressed by precluding the initiation of therapist-patient sexual contact until a substantial period of time has elapsed after the end of treatment. We suggest 1 year as a period that appropriately balances the interests involved, although we recognize that any line drawing is largely arbitrary (56). During this 1-year period, no social contact or communication at all (other than incidental contact) would be permitted between therapists and patients who later begin sexual relations. If social contacts occur and the parties later desire to begin an intimate relationship, a 1-year interval would still be mandatory before sexual contact took place.

How would a waiting period eliminate the problems that are likely to arise if sexual contact is permitted shortly after the end of treatment? As already noted, sex between a therapist and former patient most resembles sex during the therapeutic relationship in the possibility that the patient's decision-making ability will be impaired as a result of the transference. Although transference may never disappear, experience suggests that its force diminishes when therapist and patient are separated for a period of time (56). Patients thereby are afforded an opportunity for reflection on their attraction to their therapists and are likely to be free of possible coercive pressures. Therapists too are given a substantial period to consider the desirability of involvement with their former patients.

The extent to which sexual contact is the product of a hasty infatuation on the part of patients and/or therapists is suggested by data from a study indicating that when therapist-patient sex occurred during therapy, it began during the first 6 months in 55% of the cases and within the first year in 77% of the cases (47). A study of sexual contact beginning after the termination of therapy (57) showed that it began in the first month after termination in 18% of the cases and in the first 6 months in 63% of the cases. The likely effectiveness of

a waiting period in diminishing this impetus toward sexual contact is illustrated by our experience: in our combined experience of more than 100 cases of sexual contact between therapists and patients or former patients on which we have been consulted, we have seen only one case in which sexual contact with a former patient began more than 1 year after the termination of treatment. The Minneapolis Walk-In Counseling Center, which has evaluated more than 2,000 cases of therapist-patient sexual contact, reported that fewer than 1% of the cases seen there involved contact begun more than 1 year after termination (G. Schoener, personal communication, Jan. 15, 1991). Additional systematic data on this point would be desirable, but in their absence a blanket rule prohibiting contact for at least 1 year appears to provide an adequate buffer.

A substantial waiting period should also mitigate other problems associated with sexual contact soon after termination. Therapists will be less tempted to terminate treatment solely to engage in sex, a frequently voiced concern (39), or to use the therapy itself for the purpose of seduction. It has been suggested that posttermination sex might in itself cause patients to distort their presentations to make themselves appear more attractive as future partners, but this seems quite unlikely if they have to wait a year to begin the relationships (39).

Is a fixed waiting period, such as the one we propose, superior to a more flexible approach, such as that suggested by the AMA (9) or embodied in the Minnesota statutes (19, 27) (the latter permit sexual contact only when it is clear that the patient is no longer "emotionally dependent" on the therapist)? We believe it is superior in several respects. First, therapists and patients who wish to initiate social relationships will know clearly in advance when they will be free of sanctions for doing so. That clarity is now lacking in many approaches, including the American Psychiatric Association's annotations to the code of medical ethics (1, 11). Second, it appears to us nearly impossible to determine retrospectively, when a legal or administrative action is brought, whether a former patient was acting primarily from transference-based or autonomous motivations. The fixed waiting period eliminates the battle of the experts, in which neither side is able to offer reliable data, that would inevitably accompany an attempt to establish emotional dependence.

A different kind of flexible approach has also been suggested. Some experts have recommended that therapists who desire sex with their patients terminate treatment, refer the patients to other therapists, and perhaps enter into therapy themselves (58). The implicit rationale appears to be to encourage both parties to "work through" the presumably neurotic basis for their attraction. But the end point is unclear. If the desire for a relationship on both sides remains, after how much therapy can it be initiated? Can the parties continue social contact in the meantime? Therapy may be useful in these cases, but without a definite, substantial waiting period or a clear idea of how much therapy is enough, the decision to enter into a sexual relationship remains

susceptible to the transference, coercive, and fraudulent influences we seek to avoid.

As we envision it, our proposal would cover all treatment provided by psychiatrists and nonmedical psychotherapists. Two objections can be raised to such a uniform approach. First, it might be argued that psychiatrists in particular engage in a variety of relationships with patients and that it is unfair to treat them all the same. The nature of the psychiatrist-patient relationship may differ markedly from case to case, particularly in regard to the crucial issues of transference and the capacity for coercion, depending on whether the psychiatrist is offering psychoanalysis, ongoing prescription of medication, or brief consultation. Greater leniency in initiating posttermination relationships might be permitted when factors that would distort patients' decision making have been minimized. We recognize the force of this contention but believe distinguishing among psychiatrists' functions in this way would be extremely difficult. At what point, for example, does a psychiatrist who officially only prescribes medication, but talks sympathetically with the patient whenever they meet, cross the line into a psychotherapeutic relationship? We favor the simplicity of a uniform rule, while leaving open the possibility that future research on variations in psychiatrist-patient relationships might allow meaningful distinctions.

A second objection might be that by dealing with all patients similarly we are ignoring the special vulnerability of particular groups. Some commentators (46) have argued that certain classes of patients should be excluded permanently from the possibility of posttermination sexual relationships. These might include patients who have been involved in long-term dynamic psychotherapy, psychotic patients, or those who have come for help in dealing with such problems as promiscuity or the consequences of past sexual abuse. This argument seems particularly potent regarding the latter categories. Individual jurisdictions might well want to experiment with creating an absolute ban for groups of patients whose vulnerability is less likely to diminish over time.

Is an absolute ban for all patients a simpler and more desirable approach? Several authors (5, 39) have analogized therapist-patient sex to parent-child incest, maintaining that, just as the latter is not justified after the child has left the home, so the former ought to be precluded forever. This comparison seems to us to be misguided. Treatment and the obligations it imposes on the therapist are time limited; parenthood is not. As much as psychodynamic theory suggests comparisons between therapist and parent, it is important to recognize, as we encourage our patients to do, that in reality they are not the same. Although an absolute ban, if observed, would afford complete protection from the negative consequences of sexual relationships between therapists and former patients, it would do so at the cost of precluding relationships that may involve no more problems than many relationships routinely sanctioned in our society. A mandatory waiting period

should provide many of the protections of an absolute ban without contradicting our usual respect for people's right to choose with whom they will associate, as embodied in our Constitution and upheld by the courts (40, 59).

This approach could be embodied in the law in several ways. Criminal sanctions, which imply that society has concluded the action in question is morally reprehensible in all circumstances, are, from our perspective, unwarranted for posttermination sexual contact. Civil sanctions would be more appropriate; specific statutes would create a cause of action for a former patient who could demonstrate harm as a result of sexual contact with a licensed or unlicensed therapist that occurred within 1 year of termination of therapy. Licensing boards could implement administrative sanctions for violations of the 1-year rule without a showing of harm to the former patient. They might also promulgate regulations regarding documentation of the termination of therapy and the 1-year waiting period. This approach would not preclude them from experimenting with additional requirements, such as referrals for both former patient and therapist to independent therapists of their own for minimum periods of time.

Professional societies could include the requirement of a strict waiting period in their ethics codes. They also provide an ideal forum for working out the fine points of such a system. Among the questions they might address are, How should the end of treatment be defined? How can waiting periods be monitored? Is therapy helpful for the former patient and/or the therapist during the waiting period? Can different rules be developed for different types of treatment? Should there be some patients with whom sexual contact is absolutely prohibited, e.g., those seeking treatment for promiscuity or past sexual abuse?

Our goal in offering this proposal is not to encourage sexual contact between psychotherapists and former patients. Even when it is not sufficiently objectionable as a matter of social policy to warrant prohibition, it is not likely to be an ideal choice for either party (39). Recognizing, however, that such episodes will occur, we are compelled to consider what policies might be most consonant with the usual approach of our society to consensual sexual relations and yet responsive to legitimate concerns about harm and unfairness to former patients. We believe the system we suggest achieves a reasonable balance of interests in this difficult area.

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Dopamine in Schizophrenia: A Review and Reconceptualization

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***Objective:** The initial hypothesis that schizophrenia is a manifestation of hyperdopaminergia has recently been faulted. However, several new findings suggest that abnormal, although not necessarily excessive, dopamine activity is an important factor in schizophrenia. The authors discuss these findings and their implications. **Method:** All published studies regarding dopamine and schizophrenia and all studies on the role of dopamine in cognition were reviewed. Attention has focused on post-mortem studies, positron emission tomography, neuroleptic drug actions, plasma levels of the dopamine metabolite homovanillic acid (HVA), and cerebral blood flow. **Results:** Evidence, particularly from intracellular recording studies in animals and plasma HVA measurements, suggests that neuroleptics act by reducing dopamine activity in mesolimbic dopamine neurons. Post-mortem studies have shown high dopamine and HVA concentrations in various subcortical brain regions and greater than normal dopamine receptor densities in the brains of schizophrenic patients. On the other hand, the negative/deficit symptom complex of schizophrenia may be associated with low dopamine activity in the prefrontal cortex. Recent animal and human studies suggest that prefrontal dopamine neurons inhibit subcortical dopamine activity. The authors hypothesize that schizophrenia is characterized by abnormally low prefrontal dopamine activity (causing deficit symptoms) leading to excessive dopamine activity in mesolimbic dopamine neurons (causing positive symptoms). **Conclusions:** The possible co-occurrence of high and low dopamine activity in schizophrenia has implications for the conceptualization of dopamine's role in schizophrenia. It would explain the concurrent presence of negative and positive symptoms. This hypothesis is testable and has important implications for treatment of schizophrenia and schizophrenia spectrum disorders.*

(Am J Psychiatry 1991; 148:1474-1486)

When initially conceived, the dopamine hypothesis of schizophrenia posited that schizophrenic illness is a manifestation of a hyperdopaminergic state (1). The foundation of this hypothesis was mainly indirect evidence gained from the study of dopamine antagonists and agonists. Specifically, the ability of neuroleptics to displace dopamine antagonists in vitro robustly correlates with the clinical potency of these agents (2, 3). Conversely, drugs that increase dopamine activity generally worsen the symptoms of schizo-

phrenia (4-7). In the last decade faults with the dopamine hypothesis have been described as data have accumulated that are inconsistent with the notion of hyperdopaminergia in all schizophrenic patients. For example, a substantial proportion of schizophrenic patients are resistant to treatment with neuroleptics, suggesting that other neurochemical systems may have a pathogenetic role in these patients. Furthermore, schizophrenic-like symptoms are rarely, if ever, induced in nonschizophrenic individuals when they are administered drugs that augment dopaminergic activity. Moreover, neuroleptics are only partially effective in alleviating the negative, or deficit, symptoms of schizophrenic patients (8), particularly after resolution of the acute phase of the illness. This, in turn, suggests that deficit state symptoms may be unrelated to excessive dopamine activity. It has also become evident that a hypothesis of excessive dopamine activity in all brain regions of schizophrenic patients is untenable. The results of post-mortem (9-14) and cerebrospinal fluid

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Supported in part by Schizophrenia Biological Research Center grant 4175-020 from the U.S. Department of Veterans Affairs and by grant MH-37922 from NIMH.

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TABLE 1. Post-Mortem Studies of Dopamine and HVA Concentrations in Brains of Schizophrenic Patients^a

Study	Subjects	Site	Results	
			Dopamine or HVA	Comparison
Reynolds (12)	SCZ (N=22), NC (N=19)	Amygdala	Dopamine	SCZ>NC; SCZ: left>right
Iacopoulos et al. (14)	SCZ-on (N=18-25), SCZ-off (N=3), NC (N=20-28)	Temporal cortex	HVA	SCZ-on>SCZ-off=NC
		Cingulate cortex	HVA	SCZ-on>SCZ-off=NC
		Frontal cortex	HVA	SCZ-on>SCZ-off=NC
		Putamen	HVA	SCZ=NC
Toru et al. (30)	SCZ-on (N=5), SCZ-off (N=5), NC (N=10)	Caudate	Dopamine	SCZ-on=SCZ-off=NC
			HVA	SCZ-on>SCZ-off=NC
		Accumbens	Dopamine	SCZ-on=SCZ-off=NC
			HVA	SCZ-off>SCZ-on=NC
Mackay et al. (31)	SCZ (N=34), NC (N=37)	Accumbens	Dopamine	SCZ>NC
		Caudate	Dopamine	SCZ=NC
Owen et al. (32)	SCZ (N=15), NC (N=15)	Caudate	Dopamine	SCZ>NC
		Accumbens	Dopamine	SCZ=NC

^aSCZ=schizophrenic patients, NC=normal comparison subjects; "on" and "off" indicate whether or not the patients were receiving neuroleptic treatment.

(CSF) (15) studies of dopamine metabolites do not make a convincing case for a homogeneous dopamine excess in schizophrenia. However, several new findings have rekindled the enthusiasm for a dopaminergic mechanism in schizophrenia:

1. Cortical abnormalities consistent with hypodopaminergic function and their possible relationship to deficit state symptoms.

2. A reciprocal relationship between cortical hypodopaminergia and subcortical hyperdopaminergia.

3. A relationship between the concentration of the dopamine metabolite homovanillic acid (HVA) in plasma, schizophrenic symptoms, and responsiveness to neuroleptics.

All these findings, both supporting and refuting a role for dopamine in schizophrenia, will be reviewed in this article. They warrant a reconsideration of the relationship between dopaminergic activity and schizophrenia.

HYPERDOPAMINERGIA

Problems

The initial evidence that abnormally high dopamine activity is a pathogenetic mechanism in schizophrenia was the correlation between potency of dopamine receptor blockade and clinical efficacy of neuroleptics. However, the finding that clozapine, the only neuroleptic proven clinically effective for schizophrenic patients who are relatively refractory to other neuroleptics (16), displays one of the weakest D₂ receptor binding affinities (2, 17, 18) challenges the hypothesis that neuroleptics are effective by virtue of their D₂ receptor blockade alone. Clozapine's affinity for D₂ receptors is one-tenth that of chlorpromazine (2, 17, 18), but in the studies comparing clozapine to chlorpromazine (16, 19-22) clozapine was more effective than chlorpromazine, generally at one-half the dose.

Moreover, it has been consistently found that chronic administration of clozapine does not increase [³H]spiroperidol binding in brain tissue (23-28), implying that it does not increase D₂ receptor sensitivity. Since dopamine antagonists increase D₂ receptor sensitivity after chronic administration, D₂ blockade by clozapine must be minimal. Significantly, despite this apparent lack of potent D₂ blockade, clozapine is a very (if not the most) effective antipsychotic.

Measurement of CSF concentrations of HVA provide additional evidence that a simple excess of dopamine activity is not associated with schizophrenia. A large number of studies measuring CSF HVA have been conducted and have been reviewed elsewhere (15). Many drug-free schizophrenic patients have normal or low CSF HVA concentrations (15, 29). One of the few consistent findings is that HVA concentration negatively correlates with the degree of cortical atrophy and ventricular enlargement. Since CSF HVA levels are affected by the site of lumbar puncture, motor activity, time of day, season, age, sex, height, and diet and since most studies have not controlled for some of these factors, it is difficult to interpret these data. Nevertheless, the results of CSF studies suggest that a homogeneous excess of dopamine (metabolism) as reflected in CSF is certainly not present in schizophrenia. However, post-mortem studies examining dopamine and HVA concentrations and dopamine receptors provide more compelling evidence of dopaminergic abnormalities in schizophrenia.

Post-Mortem Studies

As shown in table 1, the HVA and dopamine concentrations in post-mortem brains of schizophrenic patients consistently show differences from the brains of normal subjects. However, the differences in the anatomical areas where the abnormalities are found are not consistent. For example, the concentrations of HVA in the caudate nucleus and nucleus accumbens

TABLE 2. Post-Mortem Studies of Dopamine Receptor Densities in Brains of Schizophrenic Patients^a

Study	Subjects	Site	Ligand	Results	
				Receptor	Comparison
Toru et al. (30)	SCZ-on (N=5), SCZ-off (N=5), NC (N=10)	Putamen	[³ H]Spiperone	D ₂	SCZ-on>NC, SCZ-off>NC
Mackay et al. (31)	SCZ-on (N=9), SCZ-off (N=3), NC (N=17)	Caudate	[³ H]Spiperone	D ₂	SCZ-on>NC, SCZ-off=NC
Seeman et al. (33)	SCZ-on (N=92), NC (N=242)	Striatum	[³ H]Spiperone	D ₂ D ₁	SCZ-on>NC SCZ-on=NC
Crow et al. (34)	SCZ-on (N=14), SCZ-off (N=5), NC (N=19)	Caudate	[³ H]Spiroperidol	D ₂	SCZ-on>NC, SCZ-off>NC
Cross et al. (35)	SCZ-on (N=8), SCZ-off (N=7), NC (N=8)	Caudate	[³ H]Flupenthixol	D ₂ D ₁	SCZ-on=SCZ-off>NC SCZ=NC
Hess et al. (36)	SCZ (N=8), NC (N=8)	Caudate	[³ H]Spiperone	D ₂ D ₁	SCZ>NC SCZ<NC

^aSCZ=schizophrenic patients, NC=normal comparison subjects; "on" and "off" indicate whether or not the patients were receiving neuroleptic treatment.

(30) and cortex (14) have been found to be higher in the brains of schizophrenic patients than in normal brains. The difference in caudate concentration was attributable to prior medication, while the finding in the accumbens applied only to the medication-free patients. Similarly, although one study (31) showed the dopamine concentration in the accumbens to be higher in schizophrenic patients than in comparison subjects, another study (32) showed more dopamine in the caudate of schizophrenic patients but not in the accumbens. Finally, Reynolds (12) reported excessive dopamine in the amygdala of schizophrenic patients, with the greatest excess in the left hemisphere. These inconsistencies may be due to differences in the medication status of the patients studied, varying analytical and statistical methods, or genuine anatomical specificity of dopamine abnormalities in schizophrenia.

Although not indicative of greater than normal dopamine turnover or activity, D₂, but not D₁, receptors have generally been found to be abnormally prevalent in the striatum of schizophrenic patients. Table 2 summarizes the dopamine receptor studies performed to date. These results have often been dismissed as simply reflecting neuroleptic treatment. However, most studies of patients who have been neuroleptic-free for at least 1 year before study or are drug naive show that these patients also have more striatal D₂ receptors than normal subjects. Other evidence from post-mortem studies, as well as preclinical pharmacological investigations, buttresses the argument that D₂ receptor excesses are not merely the result of neuroleptic treatment. A bimodal distribution of D₂ receptors in the brains of schizophrenic patients who have received neuroleptics indicates that neuroleptics do not uniformly increase D₂ receptor numbers in schizophrenic patients (33). The number of excess striatal dopamine receptors due to neuroleptic pretreatment in experimental animals is one-half of the difference be-

tween post-mortem tissue from schizophrenic and normal subjects (30, 31, 33–35). Rodents treated with neuroleptics have 30% more D₂ receptors than untreated rodents, whereas the brains of schizophrenic patients have 50% to 60% more D₂ receptors than those of normal subjects. Neuroleptic-treated patients with Alzheimer's disease or Huntington's disease have 25% more striatal dopamine receptors than do comparison subjects, whereas the number for schizophrenic patients exceeds that of comparison subjects by more than 100% (33), providing suggestive evidence that neuroleptics account for only some of the excess of D₂ receptors seen in schizophrenia. One study (36) showed greater D₂ receptor density but lower D₁ receptor density in the caudate nuclei in schizophrenic patients than in normal subjects. Thus, the available data strongly suggest that D₂ (but not D₁) receptor density is higher than normal in schizophrenia and that this finding cannot be totally accounted for by medication history.

Positron Emission Tomography Studies

Positron emission tomography (PET) measurements of in vivo D₂ receptor affinity in humans have provided conflicting results. One group who studied 10 neuroleptic-naïve schizophrenic patients and 11 healthy comparison subjects, using [¹¹C]methylspiperone as a D₂ ligand, found more D₂ receptors in the patients than in normal comparison subjects (37). In contrast, when 15 (38) and 18 (39) similarly drug-naïve schizophrenic patients were studied with [¹¹C]raclopride, D₂ receptor density did not differ between the patients and normal subjects. However, an asymmetry in D₂ receptor density was found in the schizophrenic but not the normal subjects: D₂ receptor density was higher in the left than in the right putamen (39). When [⁷⁶Br]bromospiperone was used to compare D₂ receptor density

in 12 schizophrenic patients (who either were drug naive or had been drug free for at least 1 year) and 12 comparison subjects, no group differences in D_2 receptor density were found (40). However, the more acutely ill patients had a greater D_2 receptor density in the striatum than the more chronically ill patients or the comparison subjects, suggesting that D_2 receptor density may be state dependent. The conflicts in the data may be partially due to differing ligands. For instance, methylspiperone, but not raclopride, binds potently to 5-HT₂ receptors. Moreover, the methods with which the PET data were analyzed varied across studies. Finally, as the study using [⁷⁶Br]bromospiperone suggests, differences in patient groups may partly explain the different D_2 receptor densities found in schizophrenic patients. These data lead to no firm conclusions at this time.

Mechanism of Action of Neuroleptics

The original notion that hyperdopaminergia is a pathogenetic mechanism in schizophrenia was, at the very least, too imprecise. For instance, there are multiple types of dopamine receptors. D_1 receptors, which are coupled to adenylate cyclase, have a low affinity for [³H]spiperone and are located in the cortex of humans (41, 42). D_2 receptors are negatively associated with adenylate cyclase, display a great affinity for [³H]spiperone (43), are most prominent in the striatal and limbic structures in humans, and, if present at all in the human cortex, have a low density (42, 44). The D_2 receptor has recently been cloned, and two D_2 subreceptors, labeled D_{2a} and D_{2b} , have been identified (45–50). The elucidation of the pharmacological, anatomical, and physiological differences between D_{2a} and D_{2b} receptors will add further complexity to the conceptualization of dopamine neurotransmission and further weaken any simplistic notions linking the action of neuroleptics to a unitary effect on all dopamine receptors. The cloning of a dopamine receptor (51) anatomically limited to limbic areas and resembling neither D_1 nor D_2 , and consequently named D_3 , underscores the fact that the initial simplistic perception of the dopamine system urgently needs to be revised. Questions remain about which dopamine receptors are most critical to modulating the symptoms of schizophrenia, where they are located, and how they differ from dopamine receptors that are irrelevant to the actions of neuroleptics. Of particular interest in this regard are the recently cloned D_4 and D_5 receptors (52, 53). D_4 receptors have a higher affinity for the atypical neuroleptic clozapine and thus have extraordinary implications for the development of a new generation of antipsychotic drugs. D_5 receptors resemble D_1 receptors but have a higher affinity for dopamine.

Anatomically, the dopamine system consists of a number of subsystems: nigrostriatal, mesolimbic, and mesocortical. The nigrostriatal system projects from the substantia nigra (also called A9) to the neostriatum (i.e., putamen and caudate). The mesolimbic system

has its cell bodies in the ventral tegmental area (also called A10) of the midbrain and in the substantia nigra and projects to the accumbens, olfactory tubercle, and amygdala. The mesocortical system has its cell bodies mainly in the ventral tegmental area, and its neurons project to the prefrontal cortex, as well as to the accumbens, septum, and olfactory tubercles (54, 55). The effects of neuroleptics on these different dopamine neuronal systems are not equivalent. A single dose of a neuroleptic increases dopamine neuron firing in the nigrostriatal and mesolimbic dopamine systems (56, 57). This is probably due to blockade of presynaptic D_2 receptors and subsequent decreased inhibition of dopamine activity (57, 58). Chronic (3–4 weeks) neuroleptic administration decreases dopamine neuron firing in both A9 and A10 to below pretreatment levels, and this decrease can be reversed by apomorphine; this phenomenon is called depolarization blockade (58, 59). Atypical neuroleptics, i.e., antipsychotics that do not induce extrapyramidal side effects, such as clozapine, are anatomically more selective in their effect on dopamine neuronal firing than typical neuroleptics in that they induce depolarization blockade in A10 only (57–64). The particular affinity of clozapine for D_4 receptors suggests that important differences among dopamine receptors can account for some aspects of clozapine's atypicality. On the basis of these data, it has been proposed that depolarization blockade in A9 is responsible for the induction of extrapyramidal effects, while depolarization blockade in A10 leads to the antipsychotic effects of neuroleptics (61). Thus, these studies suggest that excess dopamine activity in A10, and not a general excess of dopamine activity, may be related to psychosis.

Thus, the data so far reviewed suggest that the antipsychotic effects of neuroleptics are related to a decrease in firing in *specific* dopaminergic neurons (i.e., A10) and, by inference, that schizophrenia may be related to excessive activity of these, and therefore not all, dopaminergic neurons. This possibility underscores the imprecision of the initial hypothesis that schizophrenia is related to excessive dopamine function in general. This point is made even more poignant by the elucidation of numerous dopamine receptor subtypes, whose specific roles in the modulation of schizophrenic symptoms remain unknown and are a critical area for future research.

Plasma HVA

The finding that depolarization blockade in A10 is a characteristic of all neuroleptics suggests that a decrease in dopamine firing (in A10) may be an important mechanism of action of antipsychotics. However, obtaining direct evidence linking the antipsychotic effect of neuroleptics to their effect on dopamine cell firing in humans has been impossible. Therefore, indirect measurements of dopamine activity must be obtained. Plasma levels of the dopamine metabolite HVA may be such a measure. The HVA found in plasma is

TABLE 3. Studies of Plasma HVA Concentrations in Schizophrenic Patients Before Neuroleptic Treatment^a

Study	Subjects	Mean Weeks Without Drug	Correlation of Plasma HVA With Clinical Rating or Between-Groups Difference in Plasma HVA Level
Maas et al. (69)	SCZ (N=23)	2	BPRS: $r=0.38$, NPR: $r=0.49$
Pickar et al. (71)	SCZ (N=11)	5	NPR: $r=0.81$
Sharma et al. (72)	SCZ (N=11), PSY (N=6)	2.5	BPRS: $r=-0.08$
Davis et al. (73)	SCZ (N=18)	4	CGI: $r=0.66$
Davidson and Davis (74)	SCZ (N=14), NC (N=14)	3	CGI: $r=0.51$, BPRS: $r=0.49$; SCZ<NC
Pickar et al. (75)	SCZ (N=8)	2	NPR: $r=0.82$, BPRS: $r=0.49$
Van Putten et al. (76)	SCZ (N=22)	4	BPRS: n.s.
Kirch et al. (77)	SCZ (N=22)	6	BPRS: n.s.

^aSCZ=schizophrenic patients, PSY=patients with various psychoses, NC=normal comparison subjects, BPRS=Brief Psychiatric Rating Scale, NPR=Nurses Global Psychosis Rating, CGI=Clinical Global Impression rating scale.

TABLE 4. Studies of Plasma HVA Concentrations in Schizophrenic Patients During Neuroleptic Treatment^a

Study	Subjects	Duration of Treatment	Drug and Daily Dose	Plasma HVA Change or Correlation of HVA Change With Change in Clinical Rating
Davidson et al. (66)	SCZ (N=30)	6 weeks	Haloperidol, 20 mg	Increase at day 1
Pickar et al. (71)	SCZ (N=16)	5 weeks	Fluphenazine, 30 mg	Decrease at weeks 3–5; Δ NPR: $r=0.89$
Sharma et al. (72)	SCZ (N=11), PSY (N=6)	4 weeks	Trifluoperazine, 40 mg	Same at week 4; Δ BPRS: $r=0.67$
Davila et al. (78)	SCZ (N=14)	4 weeks	Haloperidol, 10 mg	Increase at day 4; Δ BPRS: $r=-0.61$
Bowers et al. (79)	PSY (N=37) ^b	9 days	Perphenazine, 0.5 mg/kg, or haloperidol, 0.2 mg/kg	Decrease at days 7–9
Bowers et al. (80)	PSY (N=29) ^c	10 days	Haloperidol, 0.2–0.4 mg/kg	Level in responders higher than in nonresponders at baseline and 4–6 days, decreased by days 19–21
Wolkowitz et al. (81)	SCZ (N=12)	10 weeks	Fluphenazine, 27 mg, plus alprazolam, 2.9 mg	Decrease in responders, increase in nonresponders
Chang et al. (82)	SCZ (N=33)	6 weeks	Haloperidol, 20 mg	Level in good responders higher than in poor responders at baseline, decreased at weeks 2–6; increase in nonresponders at 1–2 weeks
Davidson et al. (83)	SCZ (N=20)	5 weeks	Haloperidol, 20 mg	Level in responders higher than in nonresponders at baseline; no change in nonresponders, decrease in responders

^aSCZ=schizophrenic patients, PSY=patients with various psychoses, NPR=Nurses Global Psychosis Rating, BPRS=Brief Psychiatric Rating Scale.

^bOnly four patients were schizophrenic.

^cOnly two patients were schizophrenic.

produced primarily by brain dopamine neurons and peripheral noradrenergic neurons. Secondary sources of HVA are peripheral dopamine and brain noradrenergic neurons. Animal and human studies (65–67) suggest that brain dopamine turnover is reflected by plasma HVA concentrations. Although the precise proportion of plasma HVA deriving from brain HVA has not been fully elucidated (68, 69), measurement of this dopamine metabolite in plasma of schizophrenic patients appears to be a valid method for investigating dopamine activity in this disorder provided certain conditions are met (70).

The results of studies on plasma HVA in humans are shown in tables 3–5. These findings are consistent with animal data, that is, neuroleptics initially increase and subsequently decrease dopamine firing. Thus, plasma

HVA concentrations rise dramatically during the first few days of neuroleptic treatment (66, 78). This rise in plasma HVA coincides with the increase in striatal dopamine firing observed in animals after acute administration of neuroleptics. After chronic (1 week or more) administration of neuroleptics, plasma HVA levels decrease to below baseline levels (71, 79), which is consistent with the depolarization blockade observed in animals after chronic administration of neuroleptics.

Indeed, studies examining plasma HVA concentrations in relation to response to neuroleptic treatment suggest an association between the effects of neuroleptics on dopamine activity and treatment outcome. The initial increase (78) and the subsequent decrease (71, 72, 80–83) after administration of neuroleptics are as-

TABLE 5. Studies of Plasma HVA Concentrations in Schizophrenic Patients After Discontinuation of Neuroleptic Treatment^a

Study	Subjects	Weeks Since Drug Discontinuation	Plasma HVA Change or Correlation of HVA Change With Change in Clinical Rating
Pickar et al. (71)	SCZ (N=11)	5	Increase at week 5; Δ NPR: $r=0.81$
Davidson et al. (84)	SCZ (N=24)	6	Greater change in relapsers than nonrelapsers; Δ BPRS: $r=0.49$
Glazer et al. (85)	SCZ (N=13)	3	Greater change in relapsers than nonrelapsers
Kirch et al. (77)	SCZ (N=22)	6	Same at week 6

^aSCZ=schizophrenic patients, NPR=Nurses Global Psychosis Rating, BPRS=Brief Psychiatric Rating Scale.

sociated with clinical response to this treatment. Conversely, clinical decompensation after discontinuation of neuroleptic treatment is associated with increases in plasma HVA levels (71, 84, 85).

The suggestion that the therapeutic effects of neuroleptics are due to a decrease in dopamine activity is further supported by plasma HVA studies showing that greater severity of illness in schizophrenia is related to greater dopamine turnover. As table 3 indicates, several studies have found a positive correlation between plasma HVA level and clinical severity (73–75). Three studies (72, 76, 77) did not confirm this finding. The most likely explanation for the different results across studies is the number of plasma HVA samples taken as a basis for the correlational studies. The studies using more than one sampling of plasma HVA found significant positive correlations between plasma HVA and severity of symptoms, whereas studies using a single measurement of plasma HVA did not. The studies producing significant correlations between plasma HVA and severity of schizophrenic symptoms averaged three (75), four (73), or 13 (74) plasma HVA samples, whereas the studies that produced negative findings (72, 76, 77) assessed plasma HVA only once. Repeated plasma HVA measurements in the same individual therefore appear to increase the signal-to-noise ratio for plasma HVA by reducing the intraindividual variance in plasma HVA concentration.

However, the relationship between plasma HVA and schizophrenic illness is not straightforward. In one study (74), plasma HVA levels were lower in chronic, treatment-resistant schizophrenic patients than in normal subjects, although plasma HVA levels still correlated with symptom severity. Such results are consistent with the data derived from a study of urinary catecholamines in a similar group of chronically institutionalized patients (86), in whom lower levels of urinary catecholamines were also prominent. This seeming paradox—the fact that levels of dopamine metabolites can be lower in schizophrenic patients than in normal subjects but still positively correlate with symptom severity—is a key impetus to reformulating the complex role of dopamine in schizophrenia.

Is There Hyperdopaminergia in Schizophrenia?

Although the original basis for the hypothesis that dopamine activity is higher than normal in schizophre-

nia appears questionable, recent evidence, particularly that derived from intracellular recording studies in animals and plasma HVA studies in humans, suggests that neuroleptics act by reducing dopamine activity in mesolimbic dopamine neurons. Moreover, most post-mortem studies have shown higher than normal dopamine and HVA concentrations in various subcortical brain regions and greater than normal dopamine receptor density in the brains of schizophrenic patients (which is probably not a medication effect), although in vivo D_2 receptor binding studies have provided more conflicting results. Still, direct comparisons of CSF, plasma, and urine HVA concentrations in schizophrenic patients and normal subjects do not support hyperdopaminergia and may suggest the opposite, that some brain regions could be hypodopaminergic. These apparent discrepancies may be partially explained by findings on the role of dopamine in the frontal cortex.

HYPODOPAMINERGIA AND FRONTAL LOBE DYSFUNCTION

There are data indicating that frontal lobe dysfunction may be associated with psychotic symptoms. Evidence of frontal lobe damage leading to abnormal behaviors strikingly similar to some of the more persistent symptoms observed in schizophrenia can be found in anecdotal and case series describing patients with frontal lobe injuries and primates with frontal lobe ablations (e.g., 87, 88). Although there is great interindividual variation in the severity and constancy of the symptoms that emerge in patients even with severely damaged frontal lobes, some of these symptoms bear a remarkable resemblance to the deficit state symptoms in schizophrenia. For example, orbitofrontal and anteromedial lesions often produce flattened affect.

Deficit state symptoms are thought to be enduring signs of schizophrenia and include apathy and avolition (8). Bleuler proposed that deficit state symptoms are pathognomonic signs of schizophrenia and are at the root of the poor social and work functions that characterize people with the chronic schizophrenic syndrome. Indeed, several observations from primates suggest that insufficient frontal cortical functioning is responsible for poor social skills. Monkeys with frontal lobe ablations have not only an inability to suppress

irrelevant stimuli, poor concentration, and impaired delayed response, but poor social function that is reminiscent of the deficit state symptoms which characterize schizophrenia. These monkeys have been observed to die isolated and alone after being chased from their groups by other animals (89). Also, like the symptoms of schizophrenia, which seem to emerge most prominently during adolescence, the emotional difficulties of monkeys with frontal lobe ablations appear not in infancy, but after the age of 24 months, the monkey equivalent of adolescence (90, 91). Indeed, any hypothesis involving the biological basis of schizophrenia must account for the striking prevalence of onset in late adolescence.

Frontal lobe dysfunction in schizophrenia, specifically hypofrontality, is demonstrable with measurements of cerebral blood flow (92–94). While performing the Wisconsin Card Sorting Test (95), a cognitive task linked to frontal lobe function, schizophrenic patients showed less increase in cerebral blood flow than normal subjects (96). Facility at the Wisconsin Card Sorting Test has been associated with the dorsolateral function of the frontal lobe (97, 98), and it is thought to represent the human test equivalent of the delayed response task used extensively with nonhuman primates as one of the most sensitive measures of frontally mediated cognitive function.

Of great interest is whether cortical hypofrontality could be reflected in dopamine metabolites emerging from (meso)cortical dopamine neurons. Because the mesocortical dopamine tract is relatively devoid of inhibitory autoreceptors, dopamine turnover in these neurons is far greater than in the mesolimbic neurons (99). Given the large volume and greater venous drainage of cortex than of striatum in human brain, the brain contribution to the pool of plasma and CSF HVA is likely to, at least partially, reflect frontal cortex dopamine activity. In fact, only frontal cortical concentrations of HVA significantly correlate with CSF concentrations of HVA in monkeys (100). Thus, CSF and plasma HVA must, in part, reflect mesocortical dopamine activity.

The contribution to CSF HVA of the mesocortical dopamine tract would be expected to be smaller in schizophrenic patients with cortical hypodopaminergia than in normal subjects. This hypothesis is supported by the finding that CSF HVA is lower in (some) schizophrenic patients, particularly those who respond poorly to neuroleptics, than in comparison groups (see 15). Furthermore, low prefrontal dopamine activity in schizophrenic patients could also explain the consistent finding of a negative correlation between CSF HVA and ventricle-brain ratio (101–103) and, more specifically, a negative correlation between prefrontal brain atrophy and CSF HVA (104). That cortical hypofunction is associated with low cortical dopamine activity is suggested by the finding that lack of increase in blood flow during prefrontal tasks in schizophrenic patients is strongly correlated with low CSF HVA concentrations (105). Moreover, blood flow in the pre-

frontal cortex increases in schizophrenic patients after administration of the dopamine agonists amphetamine (106) and apomorphine (107), suggesting that the hypofrontality found in schizophrenic patients can be redressed by increasing dopamine activity in the prefrontal cortex. The increase in prefrontal blood flow after amphetamine administration correlated significantly with improved performance on the Wisconsin Card Sorting Test (106), strongly suggesting that increasing dopamine activity improves cognition related to prefrontal cortical activity.

Further evidence that dopamine function may be abnormally low in (some) schizophrenic patients comes from studies examining dopamine metabolites in these patients. In addition, plasma HVA has been studied in chronically institutionalized schizophrenic patients with relatively low levels of positive symptoms and prominent deficit symptoms (74). These patients had significantly lower levels of plasma HVA than the age-, gender-, and weight-matched comparison group. This finding corroborates the low concentrations of HVA in the urine of chronic schizophrenic patients (86).

Finally, indirect evidence that dopamine activity is low in (some) schizophrenic patients is suggested by clinical similarities between schizophrenic patients and those with Parkinson's disease. The cognitive and motivational defects in patients with Parkinson's disease are strikingly similar to the deficit symptoms in schizophrenic patients. It has been suggested that these Parkinson's disease symptoms result from low cortical dopamine activity (108), and they diminish after treatment with dopamine agonists (109). Deficit schizophrenic symptoms may also improve after administration of dopamine agonists (110, 111).

Hence, the abnormally low prefrontal activity commonly revealed in schizophrenic patients may be related to the negative/deficit symptom complex and is associated with insufficient activity of mesocortical dopamine neurons.

A MODIFIED DOPAMINE HYPOTHESIS OF SCHIZOPHRENIA

Linking Hypo- and Hyperdopaminergia

The data reviewed so far suggest that schizophrenia can be characterized by hypodopaminergia in mesocortical and hyperdopaminergia in mesolimbic dopamine neurons in at least some patients. There are data indicating that the two conditions, cortical hypodopaminergia and subcortical hyperdopaminergia, may be related.

Lesions of dopamine neurons in the prefrontal cortex of rats, induced with the neurotoxin 6-hydroxydopamine, have resulted in increased levels of dopamine, HVA, and dihydroxyphenylacetic acid (DOPAC) in the striatum (112, 113) and accumbens (112–114) in most but not all (115) studies. These

lesions also resulted in an increase in D_2 receptor binding sites (112, 113, 116) in the accumbens. Moreover, lesions in the prefrontal cortex augment the responsiveness of the striatal dopamine system to amphetamine (as expressed by increased locomotor activity and circling behavior) (112) and to apomorphine (as expressed by enhanced stereotyped behavior) (117). Conversely, injection of the dopamine agonist apomorphine in the prefrontal cortex of rats reduced the levels of the dopamine metabolites HVA and DOPAC by about 20% in the striatum, suggesting that increasing prefrontal cortical dopamine activity decreases striatal dopamine turnover (117). When the cortical lesion includes noradrenergic pathways, an effect on subcortical dopamine is not found (115), pointing out the important modulatory and permissive role norepinephrine plays in the reciprocal interaction between mesocortical dopaminergic and subcortical dopaminergic activity. However, these findings have not been consistently replicated. In one study (117), surgical ablation of the prefrontal cortex did not result in an increase in striatal dopamine or DOPAC, and the behavioral response to apomorphine was not confirmed when stereotactic injections of ibotenic acid were used to destroy prefrontal dopamine fibers (118). The methods used to destroy prefrontal cortical dopamine fibers in these two studies differed significantly from those using hydroxydopamine plus desipramine and may explain these discrepant results.

Post-stroke patients provided the first evidence that low frontal cortical activity is associated with greater subcortical dopamine activity in humans. Rodents with unilaterally high levels of striatal dopamine turn away from the side with more dopamine ("contraversive turning behavior"). Thus, if cortical lesions increase striatal dopamine, unilateral cortical lesions should unilaterally increase dopamine in the striatum and thus lead to contraversive turning behavior. Indeed, 23 patients with unilateral ischemic frontal cortical lesions (119) showed more contraversive turning behavior than normal subjects. Inasmuch as contraversive turning behavior is due to asymmetrically increased striatal dopamine activity, these data suggest that cortical lesions increase striatal dopamine activity.

Thus, there are circumstances under which low prefrontal dopamine activity may lead to greater than normal subcortical dopamine turnover and D_2 receptor sensitivity. This relationship has obvious implications for a conceptualization of the role of dopamine in schizophrenia, as the data previously reviewed indicate that schizophrenia may be characterized by abnormally low tonic activity of ascending dopamine neurons to the cortex and subsequent high activity in the subcortical dopamine nuclei. This hypothesis is particularly appealing since it would explain the (concurrent) presence of negative and positive symptoms in schizophrenic patients and the finding of both low plasma HVA levels and a positive correlation between severity of psychosis and plasma HVA levels in schizophrenic patients (74). Deficit state symptoms can be

related to low prefrontal dopamine activity, low plasma HVA, low CSF HVA, and low prefrontal blood flow during frontal tasks; positive symptoms are related to high dopamine activity in A10, a direct correlation between plasma HVA and positive symptoms, and an association between higher plasma HVA concentration and responsiveness to neuroleptics.

Unanswered Questions

This review and reconceptualization of the role of dopamine in schizophrenia has repeatedly stressed that dopaminergic transmission correlates with the symptoms of the disease. In contrast, dopaminergic mechanisms have not been linked with either pathogenesis or etiology. In fact, there is compelling evidence that hyperdopaminergic transmission is unlikely to be the primary or sole event in either the etiology or pathogenesis of schizophrenia. Rather, modulation of symptoms by dopamine is more consonant with the effects of neuroleptics and the inability of enhanced dopaminergic activity to induce psychosis in normal subjects. Hence, the primary abnormality or abnormalities that make the symptoms of schizophrenia amenable to manipulation by dopaminergic neurotransmission remain undetermined.

It is possible that cortical hypodopaminergia changes a schizophrenic patient's brain in a manner that makes it vulnerable to the psychotomimetic effects of direct or indirect dopamine agonists. However, this speculation remains to be tested, and other possibilities must ultimately be considered. For example, a low concentration of 5-HT₂ receptors in the frontal cortex (120) or a dysplasia of glutamate afferents to frontal cortex (121) may be a critical abnormality that establishes the substrate necessary for sensitivity to dopaminergic manipulations.

Yet another unanswered question is the relationship between morphometric abnormalities in schizophrenia and dopaminergic neurotransmission. A consistent inverse relationship between ventricle size and CSF HVA level has been found (101–103), but more precision in linking abnormalities in brain morphology, cytology, and dopaminergic mechanisms is needed. Increasing attention will inevitably be given to hippocampal and other medial and anterior temporal lobe structures and dopaminergic innervation. Fortunately, advances in immunohistochemistry, quantitative morphology, and molecular biology make possible the simultaneous elucidation of structure and neurochemistry. The availability of adequate human tissue may be the largest obstacle to this work.

Experiments with animals (112–118) have focused on the effect of cortical manipulations on subcortical dopamine neurotransmission. They have established that in some cases subcortical dopaminergic variables can be influenced by changes in cortical dopamine concentrations. Left unaddressed is whether mesolimbic alterations can produce cortical hypodopaminergia. The answer to this question is central to elucidating the

sequence of changes in dopaminergic neurotransmission during the elaboration of schizophrenic illness. The temporal sequence has implications for whether deficit state symptoms are always a part of the premorbid state of schizophrenia or whether the first appearance of deficit state symptoms can coincide with or occur after the initial psychotic event.

Finally, an elaboration of the neurochemistry of the symptoms of schizophrenia must deal with the relationship between age and symptom onset. The onset of schizophrenia is exquisitely age dependent. As has been pointed out (122), late adolescence is a time of active modification of cortical organization and changes in dopamine concentrations. The relationship between such changes and the possible development of cortical hypodopaminergia needs to be determined. Late life is another period in which the incidence of psychosis increases. This may be related to the decrease in dopamine activity in the prefrontal cortex found with increasing age (123). Thus, late-life psychoses may also prove a fertile area in which to elucidate the role of dopamine in psychotic symptoms.

IMPLICATIONS

Treatment

It has been commonly noted that the premorbid state of schizophrenic patients is characterized by social withdrawal, isolation, and many other deficit state symptoms, although they are not as pronounced as they are after the schizophrenic illness has begun. As noted, this premorbid condition is consistent with hypodopaminergia in the cortex and raises the question of whether hypodopaminergia is an early dysfunction in schizophrenia and a harbinger of the hyperdopaminergia to follow. If true, might this stage be amenable to intervention with dopamine agonists? Since mesocortical dopamine neurons are primarily of the D₁ type, one would expect selective D₁ or D₅ agonists to be particularly helpful at this stage. Would the administration of D₁ or D₅ agonists to offspring of schizophrenic patients who display negative symptoms prevent the subsequent development of psychosis? Moreover, consistent with the finding by Jaskiw et al. (124) that increasing prefrontal cortical dopamine activity reduces striatal dopamine activity, D₁ or D₅ agonists would be expected to decrease the hypothesized excessive dopamine activity in subcortical dopamine neurons and thus be useful (in combination with traditional D₂ antagonists) in the treatment of acute psychoses as well. Preliminary data on nonresponsive patients treated in this manner are consistent with this notion (125).

Symptoms of schizophrenia can routinely be exacerbated by the administration of drugs that enhance dopamine activity (4–7). All these agents increase dopamine neurotransmission at multiple subtypes of

dopamine receptors, but is activation of all subtypes necessary? It can be argued that whereas D₂, D₃, or D₄ stimulation at mesolimbic sites would be psychotomimetic for schizophrenic patients, D₁ or D₅ stimulation may not have the same effect. The determination of the ability, or inability, of D₁ or D₅ agonists to exacerbate schizophrenic symptoms is of great theoretical interest.

Schizophrenia Spectrum Disorder

Although a premorbid schizoid state can precede a schizophrenic episode, the schizoid personality disorder can be persistent and unassociated with the development of psychosis. Nonetheless this “schizophrenia spectrum disorder” is genetically related to schizophrenia (126, 127). If schizoid individuals share with schizophrenic patients the negative symptom of asociality, it seems logical to wonder if D₁ or D₅ agonists might be an effective treatment for the schizoid personality; they might enhance sociality. Thus, a clinical trial of a D₁ or D₅ agonist offers a test of one aspect of this reconceptualized role of dopamine in schizophrenia.

Differences in the relative presence of the positive and negative symptoms of schizophrenia among the full range of schizophrenia spectrum disorders also have key implications for this reconceptualization and are a fertile area of inquiry. There may be dramatic differences in overt symptoms of psychosis between patients with schizoid or schizotypal personality disorders and patients with schizophreniform episodes or schizophrenia. In contrast, negative symptoms, such as asociality and anhedonia, are shared by patients in the schizophrenia spectrum who may differ substantially in terms of positive symptoms. This observation raises the question of whether all individuals with cortical hypodopaminergia inevitably develop subcortical hyperdopaminergia and psychosis. Differences in the reciprocal relationship between cortical and subcortical dopamine may be the reason few patients with schizoid personality become psychotic, in contrast to schizophrenic patients, who may still manifest schizoid function when in remission or residual states. Elucidating these differences could offer new strategies for developing antipsychotic drugs. Hence, comparative investigations of schizophrenia and the spectrum disorders seem valuable. Indeed, such studies might have as their goal the elucidation of the biological and environmental factors that mediate subcortical hyperdopaminergia after cortical hypodopaminergia.

Future Research

The cloning of the D₂ receptor in rodents (45) and humans (48) and the eventual cloning of the D₁ receptor will facilitate the further elaboration of the role of dopamine in schizophrenia. There are at least two D₂ isotypes. Possible differences in the neuroanatomical distribution and function between these different D₂ receptors, as well as among the likely subtypes of the D₁ receptor, need to be elucidated. Already there are

suggestions that the protein sequences of D₂ subtypes differ in the region binding G proteins (50). The possibility that D₅ receptors have a greater affinity for dopamine than D₁ receptors makes the D₅ receptor a particularly intriguing target for strategies designed to reverse cortical hypodopaminergia. Similarly, the cloning of D₃, D₄, and D₅ and the elucidation of the biology associated with them may contribute to the understanding of the reciprocal relationship between mesocortical and mesolimbic dopaminergic activity. It might even prove possible to identify the dopamine receptors most critical to the antipsychotic action of neuroleptics and to devise drugs that are far more specific, and have fewer adverse effects, than those presently available. Such a possibility is already suggested by the affinity of clozapine for D₄ receptors.

Regional differences in dopamine activity profoundly affect strategies for measuring dopamine function in schizophrenic patients. Whether dopamine activity is greater or less than that in normal subjects depends on a host of factors, including the relative contribution of the different dopamine tracts to the dopamine variable being measured in any particular patient. CSF and plasma dopamine metabolites and neuroendocrine measures linked to dopamine activity provide different windows onto dopamine systems. They should not be regarded as equivalent. Furthermore, the profile of a patient's symptoms also influences net measures of dopamine activity. Hence, not all schizophrenic patients show the same differences in dopamine activity compared to comparison groups. For example, older schizophrenic patients, who have fewer positive symptoms and relatively more profound deficit states, would be expected to have a very different pattern of dopamine measurements than younger schizophrenic patients, who have prominent positive symptoms. There is in fact evidence for a 2.2% decrease in D₂ receptor density per decade after the age of 20 (128). Moreover, dopamine synthesis diminishes with age (because of decreased tyrosine hydroxylase activity) in humans (for review, see 129). Past contradictory findings must be interpreted with these considerations in mind. Hence, studies of dopamine function in schizophrenia will have to deal with far more variables than have ever been previously considered, including symptoms and the brain regions contributing to the dopaminergic variable being measured.

Finally, it would be surprising if neurotransmitter systems other than dopamine were not involved in the pathogenesis of schizophrenia. There is, for instance, considerable evidence that noradrenergic abnormalities are present in schizophrenia (for review, see 130). A role for serotonergic abnormalities in schizophrenia has been suggested as well (see 131). As previously noted, it is difficult to induce most of the positive symptoms of schizophrenia in nonschizophrenic individuals through the administration of dopaminergic enhancers. In contrast, schizophrenic patients routinely experience exacerbations of symptoms when they receive either direct or indirect dopamine ago-

nists. Thus, neurotransmitter or neuromodulatory abnormalities that are extradopaminergic must be invoked to explain the fundamental difference between schizophrenic and nonpsychotic individuals and to account for the sensitivity of schizophrenic patients to manipulation of dopaminergic neurotransmission.

Nevertheless, the evidence that abnormalities in the dopamine systems affect the modulation of the symptoms of schizophrenia is compelling. Many aspects of the reconceptualization of the role of dopamine in schizophrenia are testable. We hope these ideas will renew interest in the relationship between dopamine and schizophrenia and stimulate investigation of many of the concepts that arise from this reconceptualization. Undoubtedly, many of these notions will prove overly simplistic, but the gathering of more data will, by further reformulations, inevitably bring us closer to an understanding of the pathophysiology of schizophrenia.

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Is the Poor Sleep of Shift Workers a Disorder?

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***Objective:** The purpose of this article is to describe the impact of shift work on sleep, as recently acknowledged in official nosologies of sleep disorders, and to discuss whether sleep altered by shift work actually constitutes a disorder. **Method:** The authors review subjective responses to recent survey questions about sleep and polygraphic measurements of sleep in shift workers and describe sleep clinic experiences with complaints related to shift work. **Findings:** Shift work entails wide variation in work schedules, sleep quality, and worker tolerance and a high prevalence of night-shift sleepiness. It probably affects rates of drug use, health status, and family organization. Clinical presentations were rare, highly varied, and empirically treated. The United States, unlike other countries, has no legal restrictions on shift work. **Conclusions:** As a clinical phenomenon, sleep altered by shift work is common and varied, probably expresses nonphysiological sleep-wake scheduling, and is little treated. Further study of its health effects and consideration of whether it is a "disorder" or a "problem" seem warranted. (Am J Psychiatry 1991; 148:1487-1493)*

Because of continually changing work schedules, shift workers contend with irregular sleep schedules and frequent readaptation periods. *DSM-III-R* contains a diagnostic category for "sleep-wake schedule disorder, frequently changing type" (pp. 306-307) that refers specifically to shift work. More than one-quarter of U.S. workers work at least occasionally on night shifts (1), and the majority of rotating and night workers experience poorer sleep than day workers. These individuals rarely come to sleep disorder clinics, however, which suggests that shift workers generally accept the sleep problems inherent in their schedules and that those who are totally intolerant of shift work select other occupations. Despite this self-selection, shift work may be a major cause of suboptimal sleep quality. This article reviews the reported sleep difficulties of shift workers.

Webb (2) has questioned whether a sleep problem is the same as a sleep disorder. This bears on whether the expected sleep difficulties connected with night work should be termed a "disorder."

One might consider poor sleep a hazard of shift work, analogous to the hazards of other work, such as coal mining, asbestos processing, or virus research. But the hazards of these occupations are really increased risks, for injury and/or infection, which employers and legislators seek to prevent. The sleep hazards of shift work seem to be more accepted, perhaps because they are considered to be the fault of the worker or a disorder rather than a natural

consequence of the work schedule. It seems a silent judgment that sleep problems are rarely discussed in the literature on industrial medicine and that no systematic research on the presumed sleep problems of sleep laboratory personnel has been published by sleep researchers, who are in a good position to observe them. It may be that shift work sleep disorder can be likened to all-night-studying disorder or having-a-newborn-child disorder; that is, it is a creature of definition.

Definitions aside, night work does impair sleep quality and quantity. Since individuals vary in their sleep requirements, the psychological cost of night work probably depends, among other things, on one's tolerance for impaired sleep. In disturbances involving frequently shifting sleep-wake schedules, altered sleep patterns are entirely provoked by the schedules imposed on otherwise normal individuals. Since these disturbances are seen with great frequency, it becomes questionable whether they are abnormal. Rather, they might be defined as the expected consequences of the scheduling. No other sleep patterns have as much potential for being considered in labor law, and therefore the way in which sleep patterns related to shift work are defined may be of consequence.

TOLERANCE FOR SHIFT WORK

Findings of Questionnaire Studies

Fifty-two shift-working professional engineers who kept 10-week sleep charts slept an average of about 60 minutes more during their off-duty days than their colleagues who were not shift workers (3). They took more naps, which were of longer duration, than the compari-

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son group, but the magnitude of the difference was small, e.g., 7.0 and 5.4 naps, respectively, per 10 weeks.

Workers who rotated among three shifts reported sleeping best when they were on the afternoon shift and worst when on the night shift (4). It should be noted that the morning shift of these respondents began at 4:45 a.m. Two-shift workers also had their best sleep when working afternoons. Daytime (7:00 a.m. to 4:00 p.m.) nonshift workers had complaint levels between those of the afternoon and night workers.

Poor quality of sleep was reported by 65% of workers on shifts that continually rotated to earlier starting times, compared with 20% of nonrotating workers with comparable jobs (1). When a work schedule was redesigned to progress to later rather than to earlier shifts every 21 days instead of every week, the production of the plant increased. Thus, the direction and the frequency of work shifts may determine how much impairment is induced by shift work.

The tolerance for different shifts also depends on whether individuals are "morning people" or "evening people." For instance, in a study of 37 computer operators alternating among shifts beginning at 4:00 a.m., noon, and 8:00 p.m., the night shift was associated with the worst sleep-wake patterns of the morning types ("larks"), who slept best when they were on the morning shift (5). Evening types ("owls"), however, slept best when they were on the night shift. When ergometer measures of heart rate while bicycling were used to determine physical fitness, fitness was lowest in workers on the night shift, but the evening types were least fit at the beginning of the morning shift.

Quoting primary sources such as in-house publications and doctoral dissertations, Rutenfranz et al. (6) stated that about 20% of 9,000 shift workers surveyed had difficulty adapting to night work. There were many complaints of noise during daytime sleep hours because of children, traffic, aircraft, and telephones, as well as the expected sleep disruptions resulting from unadjusted circadian systems.

More recently, Dumont et al. (7) canvassed 426 nurses with questionnaire items pertaining to the quality of sleep and vigilance. From a principal components analysis they extracted questions that loaded on a quality-of-sleep factor. An insomnia index was calculated for each respondent by multiplying the magnitude of her scale response to each item by its factor loading from the analysis. This index increased stepwise with the number of years on the night shift, except for those with the most night work (mean=13.4 years), who had the lowest score. Among this group that was most tolerant of night work, there presumably was a higher proportion who chose to remain in night work despite having sufficient seniority to bid for day work.

The schedules of air flight crews provide a particular example of continually changing work shifts. Some flight crew members maintain their home sleep-wake schedules while flying, and others schedule themselves according to local time. Thus, "jet lag" is in many ways analogous to shift work, although it benefits from all

time cues (e.g., sunrise, sunset) that encourage adjustment, and it is usually acute rather than chronic. Czeisler and Allan (8) stated that both jet lag and shift work require shifting of the circadian phase. Wever (9) stated that the problems of readjustment of rhythms after schedule displacement may apply to shift work as well as to jet lag. Flight crew members can probably remain on their home time only temporarily at their destination, because time cues such as the light/dark cycle and social schedules will influence them. Flight configurations and length of stay at the destination vary in the same way as work shifts do; thus, jet lag and shift work are generic terms for ranges of overlapping phenomena.

Crews on transmeridian flights have been extensively studied during shift work. Hauty and Adams (10) found an increase of fatigue in these individuals after multiple time zone shifts that did not last as long as the resynchronization period for calcium or steroid excretions. Kurosaki et al. (11) reported more sleepiness and diminished mood in crew members after polar flights from Tokyo to London. A large questionnaire study of 312 Air France personnel (12) revealed that a variety of adjustments were made after long transmeridian flights (e.g., remaining on the departure city time or going to bed early in local time after a westward flight). After they had accommodated to American time, poor sleep was reported by 75% of personnel readapting to Paris time, but most slept well by the second night, even though steroid and calcium excretions took 4 or 5 days to resynchronize with local time.

To summarize the findings of questionnaire studies, it seems that different shift schedules induce different alterations in sleep patterns; that such alterations induce insufficient sleep in some persons, especially during an adjustment period after shift rotation; that subjects associate the night shift with their worst sleep; but that some workers feel that they sleep better when they are on continued night shift. Thus, shift work induces heterogeneous responses.

Results of Objective Measurements

An early polygraphic study of nurses (13) found that day sleep after night work was shortened by an average of 104 minutes compared with night sleep after day work. In contrast, 10 night-working air force corpsmen showed little sleep disturbance, although abnormal polygraphic patterns such as frequent transitions between sleep stages were observed (14). The dim light conditions of the Antarctic winter gradually diminished slow wave sleep in all workers studied (15). In this setting, night work induced diminished sleep with early rising for weeks after return to the day shift, coinciding with an advance in the timing of the daily melatonin rhythm (16). Among 16 locomotive engineers with irregular work hours, day sleep after night sleep was about 3.3 hours shorter than night sleep, with shorter sleep onset times and less stage 1, stage 2, and REM sleep (17).

Day sleep is longer after longer periods of night sleep deprivation, but nevertheless it is truncated, e.g., 2.9

hours after 50% deprivation and 4.5 hours after 100% deprivation (18). An unusual work pattern in Japan consists of a 24-hour work shift, allowing 3.5 hours sleep, alternating with 24 hours off. On days off, day sleep beginning at 11:00 a.m. was shorter and included more awakenings and more stage shifts than night sleep (19). Among 19 men on rotating work shifts, the length of night sleep progressively decreased the later in the night it began (20). Slow wave sleep increased as the prior wake period was lengthened, in contrast to REM sleep, which was present in greater amounts at the end of the night regardless of bedtime or prior wakefulness.

To summarize, almost every polygraphic study has revealed marked changes in sleep pattern associated with shift work.

SLEEPINESS

However well or badly workers sleep at home when they are on the night shift, many of them feel sleepy at work. When asked, "Out of a week of day shifts, how many times do you usually nod off or fall asleep while at work?" 23% of industrial workers reported that they slept sometimes, whereas on analogous questions 20% and 53% responded that they fell asleep on evening and night shifts, respectively (21).

Of 1,000 locomotive engineers on day trips, 8% admitted "dozing off on most trips" and 23% at least once; for night trips, 11% and 59% gave such responses (22). Of monitored locomotive engineers on night trips, 60% manifested signs of sleepiness, such as increased alpha activity and slow eye movements; 20% fell asleep while on the job. On the basis of these and other polygraphic studies, Akerstedt estimated that 75% of night shift workers were sleepy every night (22). Thus, the sleepiness of night workers seems to be a normal if not a desirable phenomenon.

AGE AND TOLERANCE FOR SHIFT WORK

The night shift sleep pattern is widely attributed to inertia of the temporally fixed propensity for sleep onset (23) in association with rapid changes in schedules. Experimenters have observed that the length and organization of sleep depend on the phase, ascending or descending, of the circadian temperature cycle in which sleep begins (24, 25). The temperature cycle itself shows delayed peaks and flattened amplitudes in night workers (26), implying dysregulation of bodily timing mechanisms.

In practical terms, the weaker internal circadian synchronization of older people (27), plus their tendency to retire and arise early (despite the morning sleep demands of the night worker [19]), may explain why night work is less tolerated with advancing age. This may also account for the relative paucity of sleep abnormalities found in young subjects whose sleep had been shifted either by night work (14) or experimentally

(28), compared with older shift workers, who had polygraphically demonstrated lower-quality sleep after night work than younger workers (17, 19). Thus, inability to tolerate night shift work may be likened to the gradually decreasing tolerance for physically demanding work of all kinds that affects greater numbers of the population with advancing age. In any case, as-yet undefined intolerances of temporal relocation of work hours (e.g., lessened sensitivity to external pacemakers or slowness of temporal reentrainment) as well as the earlier sleep phase of advancing age predispose to sleep disturbances.

OTHER PROBLEMS WITH SHIFT WORK

There may be other explanations for intolerance of shift work, however, since dislocation of circadian rhythms affects all shift workers, but only 20% of them tolerate it poorly, and these are not necessarily the oldest 20% (6, 29). In an overview of shift work, Rutenfranz (30) pointed out that many of the nonspecific complaints of night workers, such as malaise, fatigue, difficulty concentrating, and irritability, could result from sleep loss. However, there seemed to be a specific problem with gastrointestinal disturbances. This impression is consistent with observations by Lavernhe in flight personnel (12) and Koller et al. in oil refinery workers on the night shift (31). Gordon et al. (13) found much heavier use of caffeine by shift workers, as well as significantly greater use of alcohol (16% of men on variable shifts had more than four drinks daily). In their repeated telephone interviews with more than 2,500 workers, these investigators also found more job stress, severe emotional problems, and, not surprisingly, more indigestion.

Reviewers have explained some of the distress of shift work as being due to social factors, e.g., frequent absences from the family, insufficient recreation, and disruption of family organization (32, 33). Among workers at a Swedish paper mill, shift workers had twice the divorce rate of day workers (34); a lesser increase (40%) was found by Tepas et al. (35) in a survey of 149 U.S. workers. There are many possible explanations for the relation between shift work and divorce, but these have yet to be elucidated. Some afternoon and evening shift workers are single parents who report that their work schedules make child care easier (35).

The prevalence of actual health problems among shift workers, as distinct from their questionnaire responses, has failed to define health problems related to shift work. Epidemiological surveys of 8,603 men working shifts for 10 or more years showed no excess deaths nor any other apparent health effect of shift work (36). Studies of 6,385 day workers and 7,963 shift workers (29) revealed consistently less absenteeism among the shift workers, despite the fact that 60% of them complained of sleep problems and 35% had gastric complaints. Those with peptic ulcers who were transferred to day work, however, had the same incidence of ulcers as day workers.

There is some concern that such epidemiological studies have insufficiently accounted for dropouts or have compared the health of shift workers with national average disease rates rather than with the health of other workers (34). Several studies suggest that gastrointestinal and cardiovascular disease rates are higher in shift workers (31, 34). Consistent with this notion is the finding of increases in triglycerides and epinephrine excretion during a 4-week counterclockwise shift rotation in comparison with a clockwise rotation, which is more congruent with circadian predilections (37). Thus, the subjective complaints of shift workers could reflect pathophysiological processes that translate into actual illness for some of them.

The literature on shift work sleep disorder seems sparse in proportion to the vast numbers of shift workers. Any sleep disturbance is heterogeneous in the sense that work schedules vary widely in design and reactions to shift work vary from intolerance to preference. The night shift seems most associated with health complaints and sleepiness of which workers often do not complain. But dislocation of circadian rhythms, augmented daytime noise, and heavy use of stimulants may lessen sleep quality and worsen sleepiness.

LEGAL AND HEALTH POLICY ASPECTS

Perhaps in keeping with the general *Zeitgeist* in the United States that intolerance of shift work is a disorder of the individual rather than a problem inherent in the system, U.S. government intervention in this area has been minimal. The implicit approach has appeared to be that sleep problems related to shift work indicate a disorder or illness, which should cause the individual worker (now designated a "patient") to seek medical help or switch to day work. The problem with such a view for many shift workers is that day-work alternatives are absent and therapeutic resources are minimal.

Beyond theoretical or general discussions about the desirability of regularity in the sleep-wake schedule and infrequent changes in work shifts, there is essentially no literature on the practical management of the sleep disturbances of individuals who tolerate shift work poorly but have no alternative work. Therefore, little clinical attention seems to have been paid to the person impaired by shift work, as distinct from the effects of shift work on the average worker.

The U.S. approach to shift work contrasts with that of most other Western democracies. Their approach has been that disorders related to shift work are a natural product of the work system and, thus, legislative protection for the workers involved is merited. For example, Brazilian law limits the work week to 36 hours for shift workers. French law limits shift lengths to 8 hours and the work week to 39 hours. Austrian law mandates an on-site medical officer for companies employing more than 50 shift workers in certain types of jobs and mandates additional paid days off. Germany has some of the most restrictive regulations concerning

airplane flight crews, and many Japanese companies provide special sleeping breaks for their night shift workers (38). Such legislation "evens the playing field" for the companies involved and does not appear to impede national competitiveness.

Individuals compelled against their preference to do shift work for want of an alternative may be distinguished from those who actively prefer shift work to regular day work. The design of protective legislation must take into account this distinction, so that limitations will be applied where they are needed for relief but will not be applied to the sizable minority who prefer their shift work schedules (e.g., 48% of surveyed oil refinery workers on permanent shift schedules [31]).

CLINICAL EXPERIENCES

In a sleep clinic that evaluates and follows approximately 120 new patients annually, there were five patients from 1985 through 1990 who presented with sleep disturbances associated with night shift work. We present the cases of three of them.

Case 1. Mr. A, a 30-year-old merchant sailor, worked from 3:00 to 11:00 p.m. on a harbor tugboat. He felt "all wound up" after work and suffered a 2-hour sleep onset time after retiring at midnight. Shortly after the onset of sleep, he would awake hungry. After a snack he would drift in and out of sleep until about 5:00 a.m. and then obtain solid sleep until 7:00 a.m. He drank a large mug of brewed coffee each morning and had decreased his alcohol intake from 12 beers daily to one every second day. He had nasal blockage, mouth breathing, and respiratory pauses during sleep that were noted by his wife.

Mr. A had a score of 53—well into the hyperarousal range (normal=17–36)—on a symptom questionnaire that correlates with neurophysiological indices of arousal (39). Sleep laboratory recording beginning at 1:30 a.m. showed normal sleep with quiet normal breathing and no oxygen desaturation.

The interaction of hyperarousal with caffeine, work activity, and night eating was thought to contribute to his insomnia. When discontinuation of caffeine produced no beneficial effect, triazolam, 0.25–0.50 mg, was prescribed, but this induced depression and crying spells the following day (unprecedented in our experience), which remitted when the patient stopped taking the drug. Attempts to quit night eating by gradual tapering of a preset size of his snack or switching from sweets to vegetables, nuts, or eggs did not help.

After Mr. A discontinued his clinic visits and experienced 4 more years of workday insomnia and fatigue, his work shift was switched to midnight to 8:00 a.m., after which he ate a full meal. Despite dreading worse sleep, he suddenly slept well between 9:00 a.m. and 3:30 p.m., with a nap between 8:00 and 9:00 or 9:30 p.m. Bedtimes after 11:00 a.m., however, yielded little or no sleep. He drank six cups of coffee daily. In retrospect, he had felt tense throughout the afternoon shift, but he was relaxed during the night shift. The previous insomnia problems remained unexplained. Although afternoon workers report better sleep than others (4), this patient may have been an evening type, like those who reportedly sleep best when working nights (5). Alternatively, the combination of daylight and night work may have provoked his hyper-

arousal tendency or a circadian temperature delay (40) that delayed sleep onset.

Case 2. Mr. B, a 20-year-old hospital orderly, had worked from midnight to 8:00 a.m. five times a week for 8 months and experienced sleep paralysis most nights for 4 months. He would awaken suddenly and be unable to move for as long as an estimated 15 minutes. This happened at any time during sleep, not necessarily after a dream. He had no other specific narcolepsy symptoms, felt fatigued during the day, and averaged about 3.5 hours of sleep per day in naps beginning about 5:00 a.m. and 9:00 p.m. He had slept 6 hours a night during high school. Recently, he had had frequent, severe, bifrontal throbbing headaches with photophobia and increasing watery diarrhea without blood or mucus.

Since beginning night work, Mr. B had drunk four cups of coffee and two cola drinks daily, had had a beer rarely, and had used no other drugs. He had recently begun a program of regular heavy weightlifting. His mother required about 2 hours of sleep nightly; his father and five siblings slept normally.

"Independent" sleep paralysis (i.e., existing without other symptoms of narcolepsy) is not rare (41), but it is unprecedented in our experience as a reason for sleep clinic consultation. The sleep deprivation, intestinal disturbance, and augmented use of caffeine commonly found with night work (13) were considered excitatory influences possibly causing the complaint, and these required control before further investigation for narcolepsy or other disorder was done.

A program of regular sleep from 9:00 a.m. to 2:00 p.m., with a nap from 9:00 to 10:30 p.m., on work days and sleep from midnight to 8:00 a.m. on rest days was fashioned according to discussions about sleep requirements and Mr. B's intuition and experimenting. He also gradually tapered his caffeine intake. Thereafter, a sleep chart revealed gradual diminution in the frequency of the sleep paralysis episodes until there were none when he reached a caffeine intake of one cup of coffee a day, which he continued. He now averaged 7.5 hours of sleep daily (a 26-day range was 4–12.5 hours) with a theoretically suboptimal schedule that reversed his sleep schedule on rest days. Thus, he exemplified, at first, the abbreviated sleep often associated with shift work (3) and, subsequently, the differences with which individuals adapt to shift work (42).

Case 3. Ms. C, a 40-year-old pharmacist, had suffered frequent insomnia and fatigue since she began working nights 2 years previously. She worked from 10:00 p.m. to 8:30 a.m. for 6 days and from 6:00 p.m. to 8:30 a.m. for 1 day, followed by 7 days off. She went to bed between 10:00 a.m. and 12:30 p.m. and arose between 7:00 and 9:00 p.m. during her work week and went to bed between 10:00 p.m. and 1:00 a.m. and arose between 7:00 and 9:00 a.m. during her rest week. Her night sleep was punctuated by frequent, brief awakenings, and her day sleep was punctuated by fewer, longer awakenings. She drank one or two cups of coffee at the beginning of her wake periods and from zero to three alcoholic drinks weekly. She lived alone in a dark, quiet basement apartment.

Ms. C's schedule, with a 12-hour displacement of the major sleep period each week, imposed maximum adjustment requirements on her. Treatment involved finding a regular sleep period that she could maintain daily, with shifting naps, according to her work and social requirements. Thus, she began to sleep from 10:00 a.m. to 5:00 p.m. when working and from 10:00 a.m. to 4:00 p.m. and from 4:00 to 5:30 a.m. on rest days. She also quit drinking caffeinated beverages.

Thereafter, she slept well, but the major sleep period drifted to an increasingly later time during her rest days because she failed to arise on time. The major sleep period was then shortened to 10:00 a.m. to 3:00 p.m. and the nap was increased to 2:00 to 5:00 a.m. on her rest days, according to when she felt sleepiest during the night. On this regimen, she maintained a steady sleep schedule but occasionally felt fatigued at unpredictable times on her rest days. She averaged about 8 hours' sleep per day, with a 1-month range of 1.5–14.5 hours.

The other two patients seen at the sleep clinic were sleep laboratory technicians, cognizant of sleep disorders and clinics for their relief and, thus, atypical as health care seekers. One of these patients was 26 years old, had worked 3–5 nights a week for 5 years, and suddenly had a few days of insomnia. This occurred in the setting of caffeine and methocarbamol use, recent quitting of both marijuana use and strenuous weightlifting after the onset of neck pain, and the prospect of marriage and moving from his home city in 2 weeks, as well as large differences in his work and rest day sleep schedules. Relief of insomnia came a few days after withdrawal of caffeine and methocarbamol, redesign of his sleep schedule to more regular hours, and his finding a new job.

The second of these patients was 46 years old, also worked 3–5 nights a week, slept in the morning after work nights and at night after rest days, used caffeine, and had had seasonal affective disorder with crying spells and a 25- to 30-lb weight gain in winter for 17 years. Redesign of her sleep schedule, so that she slept from 10:00 a.m. to 6:00 p.m., with a 2-hour nap beginning at 2:00 a.m. on rest days and exposure to bright light at 6:30 p.m., shifted a slump period that had previously occurred between 11:00 p.m. and 1:00 a.m. to 4:00 p.m. and brought regular sleep. Only with the addition of fluoxetine, 20 mg/day, did severe carbohydrate craving and frequent crying spells remit.

One of these technicians was referred from a nearby hospital, but the second came from a distance that required several hours' travel, having been unable to find relief of her symptoms locally. Her problems in finding help exemplify the impracticality at present of consigning shift workers with sleep disorders to the medical care system and the need for greater clinical understanding of night shift workers' sleep problems.

CONCLUSIONS

This small experience with shift workers suggests that they rarely consult sleep disorder clinics, that those who do so tend to be hospital workers, that some maintain highly varied sleep hours, and that their sleep difficulties stem from a complexity of possible causes, precluding much diagnostic generalization. Treatment consists of a jumble of empirical methods emphasizing sleep hygiene and establishment of predictable sleep hours. Outcomes vary hugely. The preference of some individuals for night work and the problems of the patients just described exemplify the wide variation

among shift workers with respect to the sleep problems previously discussed (32, 33). Future research might aim to define factors associated with tolerance of shift work and the effects of instituting measures designed to lessen the sleep difficulties associated with shift work on the complaints, morbidity rates, and production rates of affected workers. Efforts to study individuals burdened by shift work schedules and those who drop out of shift work will presumably define more specifically the clinical aspects of difficulties imposed by shift work. Given the majority of shift workers who would prefer day work (31), a possible study population is apparently at hand.

The general management of such problems is probably at best a combination of prevention (1, 43) and worker education and self-selection. The ubiquitous presence of shift work since the last century, the predominant view of it as a normal stress, the relatively late recognition of sleep-wake schedule disruption as a valid pathophysiological problem, and the relative rarity of sleep clinic treatment programs all suggest that clinical management of individual problems related to shift work is much more frequently needed than the medical literature to date indicates.

In producing criteria for shift work sleep disorder, the American Sleep Disorders Association simply defined it as any complaint of insomnia or excessive sleepiness associated with working during the habitual sleep phase, usually night work (44). It stated that "the disorder is usually able to be diagnosed by history" and that it is transient, corresponding to work schedules. When diagnosis is in doubt, a variety of investigations are suggested, but it is proposed that any sleep abnormality, rather than specific criteria, would be consistent with the disorder.

It seems that the mechanisms by which some individuals doing shift work are intolerably afflicted, some complain but continue to work, and some prefer night work remain unclear. Such mechanisms may include biological clock phenomena associated with age, morning and evening types of personality, and perhaps total sleep requirements. For the moment, any complaint of diminished sleep quality that disappears when work shifts are optimized seems to stand as the major criterion for diagnosis of shift work sleep disorder. Whether this common reaction is a "disorder" or a "problem" (2) may continue to be a matter of definition. Most employment is fraught with personal disadvantages to the worker, and some involves personal risk and thus necessitates compensation and/or protective legislation. The extent to which one of these disadvantages, shift work, accounts for diminished health is presently unknown. Although one might consider those whose poor sleep makes shift work intolerable to be patients with shift work disorder, individual limitations exclude most people from many occupations without their being considered to have a disorder. Whether the difficulties associated with shift work should be considered a disorder rather than a predictable, if problematic, response to scheduling deserves careful consideration.

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Somatization and Psychiatric Disorder in the NIMH Epidemiologic Catchment Area Study

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***Objective:** Somatization has often been viewed as a defense against awareness of emotional distress or as a masked version of depression. This report examines whether community residents with high levels of functional somatic symptoms also report overt psychological distress and whether somatization is associated with any specific psychiatric disorder. **Method:** Analyses used data from the community sample of the National Institute of Mental Health Epidemiologic Catchment Area (ECA) study, a population-based survey of psychiatric morbidity among more than 18,000 residents of five U.S. communities. **Results:** Increasing number of somatization symptoms was strongly associated with overt expression of psychological distress and psychiatric symptoms. Among ECA respondents with five or more current functional somatic symptoms, 63% reported current psychological symptoms and 50% met criteria for a current psychiatric diagnosis (compared to 7% and 6%, respectively, among those with no current somatization symptoms). Somatization symptoms showed strongest associations with anxiety and depressive symptoms, intermediate association with symptoms of psychotic disorders, and weakest associations with symptoms of substance abuse and antisocial personality. **Conclusions:** ECA study respondents with high levels of somatization symptoms typically reported overt psychological distress, especially anxiety and depression. Patterns of response do not support a dissociation between physical and emotional symptoms. Functional somatic symptoms appear to be common expressions of distress instead of defenses against awareness. (Am J Psychiatry 1991; 148:1494–1500)*

Somatizing patients present with persistent, medically unexplained physical symptoms that pose diagnostic and therapeutic problems for psychiatric and

general medical practitioners (1). These functional somatic symptoms are also a major stimulus to health care utilization (2). Although somatization disorder that meets *DSM-III* criteria is rare in the general population (3), less severe forms of somatization are common and are associated with both significant morbidity and increased use of health services (4, 5).

Traditional explanations of somatization view functional somatic symptoms as an altered expression of underlying psychiatric disturbance, most often depression (6). Somatizing patients are said to defend against awareness or expression of psychological distress by selective reporting of physical symptoms instead of emotional ones. Unexplained physical symptoms, therefore, serve as “depressive equivalents” or “masked” expressions of latent psychiatric illness.

Nemiah and Sifneos (7) described the concept of alex-

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This research is based on the NIMH Epidemiologic Catchment Area Survey public use data set, wave 1 household sample. The survey was a series of five epidemiologic research studies performed by five independent research teams in collaboration with the NIMH Division of Biometry and Epidemiology. The five research studies were carried out by Yale University, Johns Hopkins University, Washington University, Duke University, and the University of California at Los Angeles.

The authors thank Drs. Wayne Katon, Samuel Dworkin, and Richard Deyo for comments on earlier versions of this manuscript. Robert Jamieson assisted with data translation and preparation.

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ithymia to characterize a group of patients who were thought to have "no words for feelings." Although this phenomenon was originally described in patients with classic psychosomatic diseases such as hypertension and peptic ulcer (8), others have applied the concept to patients with functional somatic symptoms (9–11). These investigators have explained the physical symptoms of somatization as altered expressions of distress by patients who are unable to describe emotional states.

Previous studies have found a high prevalence of psychiatric disorder, especially depression, in clinical samples of patients presenting with unexplained physical symptoms. These investigations typically use self-report inventories and structured diagnostic interviews to compare somatizing patients to medical control patients or community control subjects. These methods have revealed elevated rates of depression in patients with chronic pelvic pain (12), disabling tinnitus (13), fibrositis (14), and chronic fatigue syndrome (15), as well as a higher prevalence of anxiety and depressive disorders among patients with atypical chest pain (16) and irritable bowel syndrome (17). Katon and colleagues (18) examined the relationship between psychiatric morbidity and medically unexplained physical symptoms in a sample of primary care clinic patients with elevated psychological distress and histories of high medical utilization. The number of functional somatic symptoms showed a linear relationship with both current and lifetime morbidity, particularly for anxiety and depressive disorders.

Population-based data also support an association between functional somatic symptoms and psychiatric illness. Escobar and colleagues (4) used data from the Los Angeles site of the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area (ECA) study to examine the relationship between medically unexplained physical symptoms and lifetime psychiatric diagnosis. Respondents with histories of depression or dysthymia reported distinctly higher numbers of somatization symptoms than respondents with histories of other psychiatric diagnoses or no psychiatric diagnosis. Swartz and colleagues (3) described a high level of anxiety and depressive symptoms among North Carolina ECA study respondents with *DSM-III* somatization disorder. Dworkin and colleagues (19) examined the relationship between pain complaints and depression in a population-based sample of subjects enrolled in a health maintenance organization. While the presence of a single pain complaint was not associated with a higher risk of depression, enrollees with multiple pain complaints had a higher likelihood of depression even after severity of pain was controlled.

This review of the existing data on the relationship between somatization and psychiatric disorder suggests the following questions: 1) Are somatizing patients unwilling or unable to report psychological distress? and 2) Is somatization associated with any specific psychiatric disorders? Data from the ECA survey are well suited to an examination of these questions. The use of a detailed structured interview yielded detailed data on

unexplained physical symptoms as well as a wide range of psychiatric symptoms and diagnoses. The large size of the survey allows stable estimates of the relationship between somatization and numerous psychiatric diagnoses and allows examination of patterns of psychological and physical symptoms reported among the full spectrum of community residents.

METHOD

ECA Study Design

This analysis used public use tapes of data from wave 1 of the ECA study (20). The ECA study was a nationwide survey of psychiatric morbidity and health service utilization carried out under cooperative agreement between NIMH and five university sites: Yale University, New Haven, Conn.; Johns Hopkins University, Baltimore, Md.; Washington University, St. Louis, Mo.; Duke University, Durham, N.C.; and the University of California at Los Angeles. Each site sampled subjects from one or more previously designated community mental health center catchment areas, geographic areas with populations of 75,000 to 250,000. Over 3,000 community residents and 500 institutional residents were studied at each site. This analysis considers only community residents.

Each site used a multistage probability sampling procedure to select households from the eligible geographic area (21). This procedure varied among sites, with some sites directly sampling households from a list of all eligible households and others using an intermediate selection of geographic subunits before selection of households. Within each household, all residents 18 years of age or older without other usual residence were enumerated. The Baltimore site sampled one resident aged 18–64 in each household as well as all additional residents over 65. Other sites randomly selected a single resident in each household, with the Durham and New Haven sites oversampling elderly residents by selecting only elderly residents from certain households. Selection of catchment area allowed intentional oversampling of blacks in St. Louis and Hispanics in Los Angeles. Overall response rates across sites ranged from 68% to 79%. Examination of early responders, late responders, and nonresponders suggests that nonresponse bias had minimal impact on prevalence estimates of psychiatric disorders or psychiatric symptoms (22).

Respondents had varying probabilities of selection because of intentional oversampling of certain groups, varying procedures for household selection, and selection of one resident regardless of household size. Each respondent was assigned a sampling weight inversely related to his or her probability of selection.

Data Collection Instruments

Psychiatric morbidity was assessed with the Diagnostic Interview Schedule (DIS), a structured interview de-

veloped by NIMH and the Washington University School of Medicine (23). The DIS uses a structured question sequence to assess the presence of *DSM-III* diagnostic criteria. Questioning follows a specified probe sequence that allows for minimum interviewer discretion. Respondents are first asked whether they have ever experienced a potential psychiatric symptom. For each positive response, interviewers follow a series of questions designed to determine whether the symptom was sufficiently severe and whether alternative explanations (medical illness, drug or alcohol use) might account for every symptomatic episode. Symptoms of sufficient severity for which alternative explanations have been excluded are classified as presumptive psychiatric symptoms (coded 5 in the scoring algorithm). For each positive symptom, interviewers at three of the five study sites also asked how recently the symptom had occurred. Computer algorithms allowed translation of symptoms into *DSM-III* diagnoses (24). The version of the DIS included in the ECA study allowed diagnoses of mania, major depression, bipolar disorder, alcohol abuse or dependence, drug abuse or dependence, schizophrenia, obsessive-compulsive disorder, phobia, somatization disorder, panic disorder, and antisocial personality.

Data Analysis

Data tapes containing the wave 1 household sample of the ECA study were obtained from National Technical Information Service, Springfield, Va. The original Statistical Analysis System data file was translated into a form readable by the Statistical Package for the Social Sciences (SPSS)-X. Analyses were conducted by using SPSS-X software (SPSS, Inc., Chicago, Ill.).

Each DIS symptom was considered positive if coded 5 in the scheme described earlier. Symptoms were considered current if they were both coded 5 and reported on recency questioning as present within the last month. For phobic symptoms, the DIS recency questions asked only whether phobia was present at the time of interview. These symptoms were considered current if coded 5 and present at the interview. Analyses of psychiatric diagnoses used diagnoses generated by DIS scoring algorithms. Hierarchical diagnostic exclusions of *DSM-III* (e.g., diagnosis of major depression precludes diagnosis of panic disorder) were not applied. Symptom counts were generated by summing all lifetime or current positive symptoms within a given diagnostic class whether or not a diagnosis was present. Symptoms from panic and phobia sections were combined to yield a single anxiety symptom count. All analyses incorporated sampling weights described earlier. Because of the multistage sampling strategy used, statistical procedures based on simple random sampling may lead to some underestimation of variance and overestimation of statistical significance. In most cases, these design effects become important only when results are of borderline statistical significance (25). Because the associations described later in this article all

greatly exceed conventional standards for statistical significance, analytic procedures based on simple random sampling should have little influence on results or conclusions.

RESULTS

We first examined whether respondents who reported large numbers of symptoms in the somatization section of the DIS avoided reporting psychological symptoms in other DIS sections. Questions about symptoms in all sections of the DIS other than the somatization and cognitive impairment sections were classified into four mutually exclusive categories: 1) emotional distress—feeling states such as sadness, depression, fear, or anxiety; 2) physical distress—physical sensations or abnormalities of physical function such as fatigue, slowing of movement; 3) thought content—abnormalities of thought such as paranoid delusions, obsessions, or compulsions (not including cognitive impairment); and 4) reported behaviors—socially proscribed acts such as fighting while drinking, using a weapon in a fight, attempting suicide.

For each respondent, the number of current positive symptoms in each category was summed to yield emotional, physical, thought content, and behavioral symptom scores. These four scores were then correlated with the number of current positive symptoms in the DIS somatization section; correlations were adjusted for age and sex. Because age showed a nonlinear relationship to symptom reporting, age adjustment was accomplished by using six dummy variables to represent seven 10-year age strata. These procedures were repeated to yield correlations of lifetime somatization symptoms with lifetime symptoms in each of the four categories listed earlier. For current data, functional somatic symptoms showed nearly identical correlations with physical and emotional symptoms of psychiatric disorder ($N=10,476$, $r=0.38$ for physical symptoms and $r=0.38$ for emotional symptoms). Correlations with thought content symptoms and reported behaviors were considerably weaker (for current data, $r=0.19$ for cognitive symptoms and $r=0.09$ for reported behaviors). Correlations for lifetime data were similar. Tests of statistical significance were not performed because the large sample size would yield highly significant p values at trivial levels of correlation.

Although these findings do not show selective avoidance of emotional symptoms associated with somatization in general, these correlations might not reveal a subset of somatizing subjects who are unable or unwilling to describe psychological distress. In order to estimate the potential size of such a subset, we first identified the DIS symptoms that most clearly expressed emotional distress (e.g., panic attacks, spells of depression, crying spells) and determined the proportion of respondents who currently reported each of those symptoms at various levels of current somatization. Results are shown in table 1. The percent of respondents

TABLE 1. Number of Current Somatization Symptoms in Subjects in a Community Sample (N=9,497) Who Had Current Symptoms or Diagnosis of Depression or Anxiety

Current DIS Symptom or Diagnosis	Number of Current Somatization Symptoms											
	0 (N=7,613)			1 or 2 (N=1,483)			3 or 4 (N=277)			5 or More (N=124)		
	N	%	SE ^a	N	%	SE ^a	N	%	SE ^a	N	%	SE ^a
Symptoms												
Panic attacks	48	0.6	0.1	58	3.9	0.5	18	6.5	1.5	32	25.8	3.9
Depressed for 2 weeks	159	2.1	0.2	124	8.4	0.7	42	15.2	2.2	37	29.8	4.1
Depressed for 2 years	55	0.7	0.3	32	2.2	0.4	15	5.2	3.3	20	16.1	3.3
Feel worthless or guilty	108	1.4	0.1	87	5.9	0.6	34	12.3	0.9	22	17.7	3.4
Crying spells	182	2.4	0.2	111	7.5	0.7	46	16.6	2.2	33	26.6	4.0
Feel hopeless	170	2.2	0.2	123	8.3	0.7	46	16.6	2.2	43	34.7	4.3
Any symptom above	538	7.1	0.3	318	21.4	1.1	115	41.5	2.9	79	63.7	4.3
Diagnoses												
Major depression	78	1.0	0.1	63	4.2	0.5	24	8.7	1.7	18	14.5	3.2
Panic disorder	8	0.1	0.0	19	1.3	0.3	9	3.2	1.0	21	16.9	3.4
Agoraphobia	352	4.6	0.2	173	11.7	0.8	74	26.7	2.7	48	38.7	4.4
Any diagnosis above	422	5.5	0.3	232	15.6	0.9	87	31.4	2.8	61	49.2	4.5
Any symptom or diagnosis above	839	11.0	0.4	439	29.6	1.2	148	53.4	3.0	92	74.2	3.9

^aStandard error of percent of cases.

reporting overt psychological distress increased steadily with the number of functional somatic symptoms. In the group reporting five or more current functional somatic symptoms (approximately the highest 1.5%), over 63% of the respondents endorsed one or more symptoms of current emotional distress. A similar analysis was conducted for the most common current psychiatric diagnoses (table 1). This yielded similar results, with almost 50% of the high somatization group having current depression or anxiety disorder. When current emotional symptoms and current psychiatric diagnoses were combined, over 75% of the high somatization group showed current overt psychological distress. Expanding consideration to lifetime symptoms and diagnoses yielded a similar pattern of results. In that analysis, 89% (N=375) of the respondents in the high somatization group reported a lifetime history of overt psychological symptoms, 57% (N=240) met criteria for lifetime psychiatric diagnosis, and 91% (N=383) reported either overt symptoms or diagnosis (data not shown). Consequently, only 9% (N=38) of the subjects in the high somatization group did not report a lifetime history of either overt psychological symptoms or psychiatric disorder.

The relationship between functional somatic symptoms and specific psychiatric conditions was examined at two levels: psychiatric symptoms and *DSM-III* psychiatric diagnoses. For the symptom comparison, current and lifetime somatization symptom counts were correlated with current and lifetime symptom counts for each psychiatric disorder. Correlations were adjusted for age and sex, as discussed earlier. Resulting partial correlations are shown in table 2. In general, somatization showed the strongest correlation with depressive and anxiety symptoms, intermediate association with symptoms of schizophrenia and mania, and the weakest association with symptoms of substance abuse and antisocial personality. Data for current symptoms showed a considerably stronger association

TABLE 2. Partial Correlations of Number of Current and Lifetime Somatization Symptoms With Numbers of Symptoms of Other Psychiatric Diagnoses in a Community Sample

Symptoms of	Correlation (r) With Somatization Symptoms ^a	
	Current (N=10,476)	Lifetime (N=17,908)
Major depression	0.41	0.35
Anxiety disorder	0.27	0.34
Schizophrenia	0.22	0.23
Mania	0.22	0.24
Antisocial personality	—	0.18
Alcohol abuse/dependence	0.06	0.11

^aAdjusted for age and sex.

of somatization symptoms with depressive symptoms than with any other diagnostic group.

To examine the association between somatization symptoms and *DSM-III* psychiatric diagnoses, logistic regression was used to determine the increase in risk for each psychiatric diagnosis associated with various levels of somatization symptoms. Logistic regression permits modeling of the effect of multiple risk factors on the probability of a dichotomous outcome (e.g., presence or absence of a psychiatric diagnosis). Results are expressed in terms of odds ratios, the ratio of the odds of a positive outcome in which a certain level of the risk factor is present compared to a reference group (typically a group in which the risk factor is absent). For this analysis, respondents who reported no somatization symptoms were considered the reference group. Results for current symptoms and diagnoses are shown in table 3; odds ratios are adjusted for age (using two dummy variables to represent three age strata) and sex. For each diagnosis, the risk of psychiatric disorder increased steadily with increasing number of functional somatic symptoms. This relationship appeared strongest for panic disorder, schizophrenia, mania, and major de-

TABLE 3. Odds Ratios for Current Psychiatric Diagnosis Associated With Increasing Levels of Current Somatization Symptoms and Prevalence for Each Diagnosis in the Highest Somatization Group in a Community Sample (N=10,326)^a

DIS Diagnosis	Number of Current Somatization Symptoms								Prevalence in Highest Somatization Group ^b (N=135)	
	0 (N=8,255)— Odds Ratio	1 or 2 (N=1,631)		3 or 4 (N=305)		5 or More (N=135)				
		Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	N	%	
Major depression	1	4.1	2.9–5.7	8.6	5.5–13.7	16.9	9.9–28.8	20	14.8	
Panic disorder	1	11.3	5.1–25.3	28.1	10.9–71.9	204	90.1–462	24	17.8	
Phobia	1	2.3	2.0–2.8	4.3	3.3–5.7	12.1	8.4–15.9	61	45.2	
Mania	1	1.6	0.3–23.8	5.9	2.4–14.5	24.0	6.0–96.5	3	2.2	
Schizophrenia	1	10.5	5.6–19.9	33.9	16.4–70.5	90.2	42.1–193	15	11.1	
Alcohol abuse/dependence	1	1.7	1.2–2.2	3.4	2.1–5.6	4.1	2.1–8.3	10	7.4	
Drug abuse/dependence	1	2.5	1.6–3.8	2.2	0.8–5.5	4.3	1.3–14.2	3	2.2	

^aWeighted data, adjusted for age and sex.^bFive or more current somatization symptoms. For these weighted figures, data are rounded to nearest whole number. Numbers and percents total more than 135 and 100, respectively, because of rounding.

pression. Respondents in the highest somatization group had a risk of current panic disorder over 200 times that of respondents in the lowest somatization group. Alcohol abuse/dependence and drug abuse/dependence showed the weakest associations. The last column of table 3 shows the current prevalence of each psychiatric disorder in the highest somatization group. Phobic disorders and depression showed the highest rates because of their strong association with somatization and their relatively high overall prevalence. An identical analysis for lifetime somatization symptoms and lifetime diagnoses yielded similar results. The pattern of odds ratios is identical, although the overall levels are slightly lower. For the lifetime analysis, prevalence rates in the high somatization group were greater because of the greater overall rate of lifetime diagnoses.

DISCUSSION

Somatization among ECA study respondents was not associated with inability or unwillingness to report emotional distress. Respondents who reported high levels of unexplained physical symptoms also reported high levels of emotional distress. Expression of overt psychological distress increased steadily with increasing number of functional somatic symptoms, and only a small minority of respondents with high levels of somatization did not report overt anxiety or depressive symptoms. Thus, masked psychiatric morbidity among the high somatization group was atypical.

Oxman and colleagues (26) used content analysis of the speech of patients with somatization disorder to demonstrate a similarly high level of reported emotional distress. Physical and emotional symptoms appeared to be closely associated types of expression of distress instead of mutually exclusive alternatives. In medical clinic settings, patients with high levels of physical and psychological distress may appear unable or unwilling to discuss emotional states because they believe physical symptoms are the appropriate prob-

lems to present to doctors. Patients who believe that psychiatric symptoms result from physical disorders may view physical symptoms as more deserving of attention. Such patients may be quite willing to acknowledge and discuss emotional difficulties when invited to do so.

These findings do not support the extension of the alexithymia concept from patients with psychosomatic disorders to somatizing patients. ECA study respondents with high levels of functional somatic symptoms typically expressed high levels of anxiety and depression. Somatizing patients and psychosomatic patients with alexithymia may actually fall on opposite ends of a spectrum of symptom sensitivity. Alexithymic patients may have as much difficulty feeling or expressing somatic distress as they do expressing emotion (8). Somatizing patients, on the other hand, may suffer from heightened sensitivity to all negative states, both somatic and psychic.

Study of the relationship of somatic distress to individual psychiatric diagnoses yields mixed results. Comparison at the symptom level suggested strongest association with depressive and anxiety symptoms. Examination at the level of psychiatric diagnosis, however, showed a surprisingly strong relationship between somatization and psychotic disorders. Studies of the validity of DIS diagnoses suggest one possible explanation. Psychiatric reexamination of ECA study respondents suggests that rarer (and more severe) psychiatric disorders may have been poorly measured (27–29). Lay interviewer diagnoses of mania or schizophrenia may simply reflect an extremely high level of nonspecific psychiatric disturbance instead of any specific disorder. Consequently, the strong associations with psychotic diagnoses may indicate a link between somatization and severe psychiatric disturbance instead of a specific association with psychosis. Thus, the combined findings for psychiatric symptoms and psychiatric diagnoses suggest that somatization is related to psychiatric morbidity in general and that this relationship is most apparent in the most disturbed subjects.

The pattern of associations may also reflect the statistical techniques used. Categorical measures of association such as odds ratios will emphasize the influence of rare conditions such as mania or schizophrenia. Correlational measures, however, will emphasize common events such as anxiety and depressive symptoms. Two exceptions to this general trend deserve further attention. Somatization symptoms show a weak association with symptom counts for alcohol abuse/dependence and antisocial personality even though these symptoms show high overall frequency. This finding suggests that somatization is truly less associated with these symptom types. The weak association of functional somatic symptoms with certain behaviors described earlier provides further support for this explanation. The diagnosis of panic disorder shows a very strong association with functional somatic symptoms despite its moderately high frequency among psychiatric diagnoses. This strong link suggests that somatization may have a specific association with panic over and above its association with psychiatric morbidity in general.

Study of current symptom counts suggests a stronger association of somatization with depression than with anxiety. The nature of symptoms included in these counts, however, may exaggerate the association between somatization and depression. The DIS depression section includes symptoms such as fatigue, psychomotor retardation, and difficulty concentrating, which might be expected to correlate with physical complaints. In comparison, anxiety symptoms routinely assessed by the DIS consist primarily of phobias, which have no apparent natural association with somatic distress. Consequently, higher correlations of somatic symptoms with depression may result in part from the particular symptoms examined.

Examination of the prevalence of various psychiatric disorders in the high somatization group shows a remarkably high rate of phobic disorders. This reflects both the moderately strong association between somatization and phobic diagnoses and the high prevalence of phobias found by the DIS in the general population. Consequently, phobias occur more than twice as often as any other DIS psychiatric diagnosis among respondents reporting the most functional somatic symptoms.

As described earlier, Escobar and associates' analysis of data from the Los Angeles ECA site (4) appears to demonstrate a specific association between somatization and depression. That analysis, however, considered all respondents with nondepressive diagnoses as a single group. A strong association of somatization trait with anxiety disorders could have been diluted by the weak association with antisocial personality and alcohol diagnoses. Depressive diagnoses would be expected to show a stronger relationship to somatization than to this mixed group.

Overall, these findings are consistent with a model of somatization as increased sensitivity to both physical and emotional distress. Investigations by Byrne et al. (30, 31), Petrie (32), and Pennebaker (33) have described individuals who characteristically amplify

physical symptoms, especially at times of emotional distress. Building on this work, Barsky et al. (34, 35) have used the term "somatosensory amplification" to describe this tendency to report high levels of somatic symptoms. Instead of viewing physical symptoms as a defense against awareness of affect, this model views physical and psychological symptoms as parallel and equally valid expressions of distress. The high correlations between psychic and somatic distress described earlier appear to support this view.

These findings have some practical implications for the care of somatizing patients. A traditional model of somatization views functional somatic symptoms as defenses against awareness or expression of psychiatric disturbance. Since unexplained physical symptoms are presumed to be masked expressions of depression and anxiety, conventional pharmacologic and psychotherapeutic treatment of these disorders should relieve the accompanying physical symptoms. One unfortunate consequence of the focus on masked psychiatric disorders is that patients sometimes feel profoundly misunderstood. Although many patients with unexplained physical symptoms will report depression and anxiety, they often view these psychiatric symptoms as consequences of physical symptoms instead of causes. When told that their physical discomfort is merely a sign of the "real" psychiatric problem beneath, such patients may respond with anger and disbelief. Reports of the difficulties encountered during psychiatric treatment of patients with medically unexplained physical symptoms illustrate this difficulty with a traditional approach (36, 37). Treatment based on the amplification model of somatization focuses on strategies to reduce underlying symptom sensitivity. Somatosensory amplification is viewed as a perceptual style amenable to change through cognitive and behavioral interventions. Barsky and colleagues (38) described a group treatment program with a psychoeducational and supportive orientation. Distraction and relaxation techniques assist patients to reduce sensitivity to bodily sensations. Cognitive interventions allow patients with unexplained physical symptoms to "reattribute" physical sensations to benign causes. The entire process considers patients' physical symptoms as genuine expressions of distress deserving of attention. Adoption of such a view might help relieve the frustration of both patients and providers.

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The Family History Method: Whose Psychiatric History Is Measured?

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Objective: The family history method, in which an informant is asked about the history of psychiatric illness in relatives, is widely used in psychiatric research. Previous research has examined the influence on family history information of characteristics of the relative. In this report, the authors seek to clarify the impact on family history reporting of the psychiatric history of the informant. **Method:** Both members of female twin pairs from a population-based twin registry were asked about the history of major depression, generalized anxiety disorder, and alcoholism in their mother and father. The authors examined twin pairs discordant for each of the three diagnoses and predicted that the affected twin would report higher rates of the same disorder in her parent than would the unaffected twin. **Results:** Twins with a history of major depression or generalized anxiety disorder but not twins with alcoholism were significantly more likely to report the same disorder in their parents than were their unaffected co-twins. **Conclusions:** For major depression and generalized anxiety disorder, a family history diagnosis appears to reflect the psychiatric history of both the relative and the informant. Caution may be needed in the interpretation of results based on the family history method, although the magnitude of this problem may be attenuated by the use of multiple informants.
(Am J Psychiatry 1991; 148:1501-1504)

Knowledge of the psychopathological status of the relatives of psychiatric patients is important in many aspects of psychiatric research and practice. Because assessing relatives directly is time-consuming, inconvenient, and often expensive, it is common practice to ask the patient or a cooperative relative about the presence of psychiatric disorders in other relatives. This technique, called the "family history method," is distinguished from direct evaluation of individual relatives, termed the "family study method."

The family history method has been extensively evaluated, especially in the assessment of major de-

pression, and results have consistently demonstrated relatively high specificity but low-to-moderate sensitivity (1-6). Further investigations have examined characteristics of the *relative* (the individual about whom questions are being asked) that affect the sensitivity of family history information. The sensitivity of the family history method increases if the relative has received treatment (especially hospitalization), has a severe psychiatric disorder or severe symptoms, or is a spouse or parent (3, 6, 7). Less attention has been devoted to examining characteristics of the *informant* (the individual giving information about his or her relatives) that influence family history information. The sole informant characteristic examined to date has been the relationship with the relative. The results of such studies have been inconsistent. For example, Thompson et al. (3) found that spouses and offspring provided more accurate family history information than parents or siblings, but Andreasen et al. (1) found parents to be better informants than siblings or offspring.

In this report, we examine the impact on family history information of the psychiatric history of the informant. We hypothesized that informants who have suffered from a psychiatric disorder would be more likely than informants with no psychiatric history to report the presence of that disorder in relatives.

Received Dec. 11, 1990; revision received April 8, 1991; accepted April 29, 1991. From the Department of Psychiatry and the Department of Human Genetics, Medical College of Virginia/Virginia Commonwealth University, Richmond; the Institute for Social Research, University of Michigan, Ann Arbor; and the Department of Psychiatry, Washington University School of Medicine, St. Louis. Address reprint requests to Dr. Kendler, Box 710 MCV Station, Richmond, VA 23298-0710.

This work was supported by grant MH-40828 from NIMH. The Virginia Twin Registry, established and maintained by Drs. W. Nance and L. Corey, is supported by grant HD-26746 from the National Institute of Child Health and Human Development and grant NS-25630 from the National Institute of Neurological and Communicative Disorders and Stroke.

John Myers, M.S., assisted in the data analysis.

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METHOD

Sample

The subjects of this study were Caucasian female same-sex twins from the population-based Virginia Twin Register, formed from a systematic review of all birth records in the Commonwealth of Virginia. Twins were eligible to participate in this study if both members of the pair had previously responded to a mailed questionnaire, to which the individual response rate was 64%. We succeeded in personally interviewing 2,163 (92.0%) of the 2,352 individuals from 1,176 twin pairs who met these criteria. The 2,163 individuals included both members of 1,033 pairs and one member of 97 pairs. Of the completed interviews, 1,932 (89.3%) were performed face to face and 231 (10.7%) were conducted by telephone. The mean \pm SD age of the sample at interview was 30.1 \pm 7.6 years and ranged from 17 to 55.

Measures, Interviewers, and Diagnostic Review

The diagnoses of major depression, generalized anxiety disorder, and alcohol dependence in the twins were made by using an adaptation of the Structured Clinical Interview for DSM-III-R (8). Each twin was also asked about a history of major depression, generalized anxiety disorder, and alcoholism in her mother and father. Family History Research Diagnostic Criteria (FH-RDC) (9) were used for major depression and alcoholism. Since no FH-RDC existed for generalized anxiety disorder, we created our own, requiring a period of at least 1 month, which was not part of an obvious justified stress reaction, in which the relative was particularly tense, anxious, or worried and either received treatment for these feelings or had three or more of the following symptoms: 1) being keyed up or on edge, 2) irritability, 3) restlessness, 4) having trouble falling asleep, or 5) tiring easily.

All interviewers underwent extensive and ongoing training during the field study, and each had a minimum of a master's degree in psychology or social work or a bachelor's degree plus at least 2 years of clinical experience. The same interviewer never interviewed both members of a twin pair.

The diagnoses of major depression, generalized anxiety disorder, and alcohol dependence (hereafter termed "alcoholism") in the twins were based on a blind review by one of us (K.S.K.), an experienced psychiatric diagnostician, using *DSM-III-R* criteria with one modification. In order to have a sufficient sample size of twin pairs discordant for generalized anxiety disorder, it was necessary to lower the minimum duration from 6 months, as specified in *DSM-III-R*, to 1 month, as specified in *DSM-III*. The family history diagnoses were assigned by a computer algorithm operationalizing the previously specified criteria.

Interrater reliability was assessed in 53 jointly conducted interviews. Each of these interviews was blindly

reviewed; the chance corrected agreement (kappa) (10) for the diagnoses of major depression and generalized anxiety disorder, as defined above, were 0.96 \pm 0.04 and 0.77 \pm 0.10, respectively. No cases of alcoholism occurred in the 53 jointly interviewed twins. The kappa value for the family history diagnoses was unity for depression and generalized anxiety disorder in the father and depression and alcoholism in the mother; for alcoholism in the father and generalized anxiety disorder in the mother the kappa values were 0.93 \pm 0.06 and 0.95 \pm 0.05, respectively.

Statistical Analysis

To explore the impact on family history information of an informant's psychiatric history, three conditions should be met. 1) The relatives assessed by the family history method should be matched or, more ideally, should be the same individuals. 2) The informants should be matched for family background so that differences in rates of illness reported in relatives do not reflect differences in familial liability to illness. 3) The informants should differ in their psychiatric history. All three of these conditions are met in our design, in which we compare the family history reports regarding parents from members of twin pairs discordant for the psychiatric disorder of interest. The significance of the association between the psychiatric history of the informant and that assigned to the parent was assessed by using McNemar's chi-square test with one degree of freedom (11). Reported p values are two-tailed.

RESULTS

As seen in table 1, our hypothesis that an informant with a particular disorder would be more likely to report that disorder in a relative was strongly confirmed for major depression and generalized anxiety disorder. For example, we found 354 twin pairs in our sample who were discordant for a lifetime diagnosis of major depression and who both provided family history information on their mother. In 181 of these pairs, both twins agreed that their mother had never had an episode of depression, and in 58 both twins agreed that their mother had been depressed. In 115 pairs, the twins disagreed about the diagnosis of depression in their mother. These 115 pairs were divisible into two groups: 1) the unaffected twin reported illness in the mother and the affected twin did not and 2) the affected twin reported illness in their mother and the unaffected twin did not. If an informant's psychiatric history does not influence reporting of family history information, these two groups should be approximately equal in size. However, the latter group (N=79) was more than twice as large as the former group (N=36), a distribution that would very rarely occur by chance (table 1).

A similar pattern of results was found for generalized anxiety disorder in the mother and father. For major

TABLE 1. Family History Diagnoses in Parents Reported by Twins Discordant for Psychiatric Illness

Lifetime Diagnosis of Twin	Parent	Number of Pairs ^a	Family History Diagnosis Reported in Parent				χ^2 (df=1)	p
			By Neither Twin	By Unaffected Twin Only	By Affected Twin Only	By Both Twins		
Major depression	Mother	354	181	36	79	58	15.34	0.0001
	Father	349	258	26	41	24	2.92	0.09
Generalized anxiety disorder	Mother	316	168	31	77	40	18.75	0.00001
	Father	306	214	22	55	15	13.30	0.0002
Alcoholism	Mother	86	70	2	4	10	0.17	0.68
	Father	85	52	4	8	21	0.75	0.39

^a Number of twin pairs discordant for a given lifetime diagnosis, where both twins provided a family history diagnosis of given parent.

depression in the father, the results were similar but far less statistically robust. For alcoholism, where the sample size of discordant twin pairs was much smaller, the results, although in the same direction, fell far short of statistical significance.

DISCUSSION

Our results suggest that for major depression and generalized anxiety disorder, family history information is substantially influenced by the psychiatric history of the informant. Informants with a personal history of major depression or generalized anxiety disorder were considerably more likely to report the same syndrome in a relative than were informants without such a history. The results for alcoholism are more ambiguous. Although our results showed no significant evidence for a similar effect, the size of our sample of discordant pairs was too small to provide a powerful test.

Our findings are explicable as part of a general cognitive mode in which the reporting of perceptions are influenced by experiences and expectations. Other studies have shown that reports on relatives for such variables as educational attainment (12), body silhouette (13), social attitudes (14), and temperament (15) are influenced by similar characteristics in the informant. In particular, our results are consistent with work in progress showing that a twin's rating of her own history of depressive symptoms influences her rating of the history of depressive symptoms in her co-twin (16).

The present results do not address the specific processes by which this pattern emerges, however. It could derive from differences in the propensity to recognize psychopathology in a relative. Personal experience with a psychiatric illness may alter an individual's ability to perceive the presence of the same disorder in a relative. Alternatively, the experience of having a psychiatric disorder may reduce the reluctance an individual feels in reporting the presence of a psychiatric disorder in a relative. It is also possible that experiencing a psychiatric disorder may have no direct effect on the reporting of psychiatric disorders in relatives; rather, the correlation between them might result from a third factor such

as cooperativeness. That is, the observed pattern of results could be obtained if some individuals accurately reported the presence or absence of personal and family psychopathology, while other individuals consistently denied both even if they were present.

Even more importantly, our results do not address the crucial question of whether individuals with a history of a psychiatric disorder are more or less accurate informants about psychiatric illness in their relatives than are individuals who report no personal psychiatric history. In other words, do the higher rates of illness reported in relatives by affected informants derive mostly from false positives reported by affected informants or from false negatives reported by unaffected informants? Assume, for example, that a personal psychiatric history changes the threshold at which an individual recognizes psychiatric illness in his or her relatives. Do informants with no psychiatric disorder have their threshold set too high so that truly affected relatives are reported to be unaffected (false negatives) or do informants with a history of a psychiatric disorder have their thresholds set too low so that relatives with normal psychological reactions are reported as having a psychiatric disorder (false positives)?

Previous research in the family history method has generally concluded that false positives are considerably rarer than false negatives (1-6). We are in the process of interviewing the living and cooperative parents of this twin sample and hope in the future to be in a position to address this critical question definitively.

A final important research question is how an informant's psychiatric history influences family history diagnoses when they are based on information from several informants. It is possible that this technique, used frequently in modern family studies of psychiatric illness, may attenuate the impact of informants' psychiatric histories on the final family history diagnosis.

CONCLUSIONS

These results, if confirmed, have important implications for the use of family history information in psychiatric research and practice because they suggest that the psychiatric history of the informant must be consid-

ered in interpreting the results of family history data. For example, one design for family history studies has been to compare the rates of a disorder in relatives of affected versus control probands by obtaining family history information from the affected and control probands, respectively. Our results suggest that positive findings in such a study may emerge because the disorder truly aggregates in families or because affected individuals more frequently report illness in their relatives than do unaffected individuals.

Before we can properly "correct" for the impact of a personal psychiatric history on family history reporting, however, further understanding of the nature of this impact is needed. For example, if unaffected informants do not recognize the presence of true psychiatric illness in relatives, might a more detailed characterization of the disorder at the time of the interview increase the level of recognition of the unaffected informant? If the problem results more from a hesitancy of unaffected informants to admit to psychiatric disorders in relatives, could techniques be used to reduce embarrassment, such as emphasizing the frequency of psychiatric disorders or allowing the relevant items to be self-administered? Regardless of the specific mechanism at work, our results suggest that the impact of an informant's psychiatric history on family history diagnoses is substantial and should be taken into account in interpreting results obtained by the family history method.

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Mood Variability: A Study of Four Groups

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***Objective:** The authors' goal was to determine whether self-rated patterns of mood regulation differed among patients with major depression, patients with borderline personality disorder, patients with premenstrual syndrome (PMS), and normal subjects. **Method:** Fourteen days of morning and evening mood self-ratings on a visual analog scale were analyzed for 65 female subjects (10 with major depression, 16 with borderline personality disorder, 15 with PMS, and 24 without psychiatric diagnoses). For each individual, the mean and standard deviation of morning and evening ratings, the mean absolute change in mood from one day to the next, and the change from morning to evening were determined. **Results:** The four groups differed significantly on every measure of mood and mood variability except diurnal variation. As expected, the group with major depression had the lowest global ratings and a low degree of variability. The group with borderline personality disorder was less depressed than the group with major depression and showed a high degree of mood variability. Auto-correlation analysis suggested that mood ratings in borderline personality disorder vary randomly from one day to the next. The mood variability over the 14 days of the patients with PMS was significantly greater than that of normal subjects. **Conclusions:** The visual analog scale can capture patterns of mood and mood variability thought to be typical of these diagnostic groups. Mood disorders differ not only in the degree of abnormal mood but also in the pattern of mood variability, suggesting that mechanisms regulating mood stability may differ from those regulating overall mood state.*

(Am J Psychiatry 1991; 148:1505-1511)

The regulation of mood is a complex and poorly understood process, with roots in individual biological factors, specific personal experiences, cultural influences, and the resulting personality and cognitive style of the individual. Several patterns of "abnormal" mood regulation appear to be well established in clinical lore. Melancholia, for example, is characterized by both depressed mood and a pathological degree of mood stability, described as "autonomous" or "environmentally unresponsive." Other disorders with a prominent affective component, such as borderline personality disorder, are characterized by highly variable and rapidly changing mood states that are exquisitely sensitive to environmental events. Disorders of mood regulation may thus involve one or more dimensions of abnormal mood: mood may be extreme, mood may show pathological variability or stability, the extremes of variability may occur over long or short time periods, and

mood may be abnormally linked to or divorced from external events.

Despite these apparently well-established features of mood disorders, there has been relatively little quantitative phenomenological research delineating patterns of mood variability in normal subjects or in patients with mood disorders. The work that has been done has sometimes failed to clearly demonstrate such "tried and true" diagnostic features as diurnal variation (worse in the morning) in melancholia (1-4).

One of the simplest methods of assessing mood is the global visual analog scale on which a subject rates current mood on an analog scale ranging from "worst I've ever felt" to "best I've ever felt." We analyzed mood data obtained twice daily over a 2-week medication-free period in normal volunteers and three patient groups chosen because of expected differences in patterns of mood variability: patients with major depression, patients with borderline personality disorder, and patients with premenstrual syndrome (PMS). We predicted that both borderline personality disorder and PMS would be associated with higher-than-normal variability in the mood ratings over the 2-week period and that major depression would be associated with lower-than-normal variability. We also examined the

Received Aug. 14, 1990; revision received April 8, 1991; accepted May 5, 1991. From the Clinical and Research Services Branch, the Clinical Psychobiology Branch, and the Office of the Clinical Director, NIMH, Bethesda, Md. Address reprint requests to Dr. Cowdry, NIMH Neuroscience Center at St. Elizabeths, Washington, DC 20032.

mean variability from one day to the next, predicting that patients with borderline personality disorder would show high day-to-day variability and patients with major depression would show low day-to-day variability. No prediction was made for PMS, since it was unclear whether the mood variability would occur as high day-to-day variability (lability) over the entire rating period or as a shift between two relatively stable mood states.

METHOD

The subjects in this study were women between the ages of 18 and 45 years who were participating in studies at the National Institute of Mental Health. All subjects were free of substantial medical illness, drug abuse, and alcohol abuse. All subjects were medication free during the rating period and, in most cases, for at least 2 weeks before the rating period. All provided informed consent for participation in research.

Four groups of women were selected for inclusion in this study. The group with major depression consisted of 10 female inpatients who had major depression diagnosed according to Research Diagnostic Criteria (RDC) (5). The group with borderline personality disorder consisted of 16 female outpatients who met *DSM-III* criteria and Diagnostic Interview for Borderline Patients criteria (6) for borderline personality disorder. In addition, they had extensive histories of behavioral dyscontrol (including suicide attempts, self-injurious behavior, rage episodes, and violence). None of the patients with borderline personality disorder was in a major depression during the rating period. Ten of the 16 patients with borderline personality disorder had experienced at least one episode of major depression according to *DSM-III* criteria. The group with PMS consisted of 15 female outpatients who were diagnosed prospectively through the use of visual analog scale ratings for 3 months. Menstrually related mood disorder was defined as a 30% or greater increase (relative to the range of severity ratings used by the subject) in mean negative mood symptom score in the week before menses over the week following menses (7). Patients were excluded from the group with PMS if they had a *DSM-III* axis I disorder or axis II diagnosis of borderline personality disorder. This group was studied before the development of criteria for the proposed diagnosis of late luteal phase dysphoric disorder (8; *DSM-III-R*). The group of normal individuals consisted of 24 female volunteers who were recruited through advertisement and through the Normal Volunteer Office of the National Institutes of Health. These women constituted the comparison group for a variety of studies of borderline personality disorder and PMS. None of the volunteers had a history of any psychiatric disorder, and none had any first-degree relatives who had been diagnosed with psychiatric disorders.

Each subject completed daily morning and evening

TABLE 1. Visual Analog Scale Self-Ratings of 24 Normal Subjects, 16 Patients With Borderline Personality Disorder, 10 Patients With Major Depression, and 15 Patients With Premenstrual Syndrome (PMS)

Variable	Normal	Borderline	Depressed	PMS
Mean				
Morning	13.21	9.25	4.87	13.06
Evening	13.67	10.27	5.23	12.87
SD				
Morning	2.24	2.83	1.67	4.54
Evening	2.69	3.18	1.75	4.55
Change				
Morning	2.03	2.96	1.51	3.19
Evening	2.59	3.23	1.66	3.18
Morning-evening difference	2.75	3.42	1.49	2.68
Diurnal variation	0.46	1.02	0.29	-0.25
Random variability ratio	0.82	0.94	0.76	0.62
Autocorrelation (r)	0.14	0.01	0.06	0.39

self-ratings of general mood on a visual analog scale, rating how she felt at the time of the self-rating on a scale ranging from "worst I've ever felt" to "best I've ever felt." Ratings were completed during a 14-day medication-free period that was selected randomly without regard for the stage of the menstrual cycle. A 14-day period was used because it was the longest period for which medication-free ratings were consistently available in all four diagnostic groups. This posed an interesting methodological issue with regard to the women with PMS, since their most marked shift in mood occurred, by definition, around the onset of menses. We chose, nonetheless, to maintain a uniform selection criterion because menstrual data were not available for patients in the other three groups and we were not able to select comparable periods around the menses for them. This decision thus provided the most conservative test of whether the group with PMS really differed from the other diagnostic groups.

Two variations of the visual analog scale were used. The first, completed by the patients with borderline personality disorder and by eight subjects in the group of normal individuals, consisted of a continuous 100-mm straight line labeled "worst I've ever felt" at the far left and "best I've ever felt" at the far right. The subjects completed this rating by making a cross-hatch line at a point along the continuum. Scores were calculated by measuring millimeters from the left end of the line to the cross-hatch mark. The second scale was designed for optical scanning of self-rating forms and consisted of 24 equally spaced circles numbered 1-24, with circle 1 at the far left labeled "worst I've ever felt" and circle 24 at the far right labeled "best I've ever felt." The subjects filled in the circle that best estimated their mood at the time. This scale was completed by the patients with major depression, the patients with PMS, and 16 subjects in the group of normal individuals. For comparability, scores from the first scale were converted to integer scores from 1 to 24 by rounding to the nearest

TABLE 1 (continued)

Kruskal-Wallis One-Way ANOVA (p<)	Wilcoxon-Mann Whitney Pairwise Comparison (p<)					
	Normal vs. Borderline	Normal vs. Depressed	Normal vs. PMS	Borderline vs. Depressed	Borderline vs. PMS	Depressed vs. PMS
0.0001	0.0002	0.0001	—	0.004	0.01	0.0003
0.0001	0.001	0.0001	—	0.002	0.03	0.0003
0.0002	—	0.05	0.0001	0.02	0.01	0.001
0.0003	—	0.04	0.0004	0.02	0.02	0.0005
0.009	0.04	—	0.01	0.02	—	0.01
0.039	—	—	—	0.02	—	0.002
0.032	0.05	0.05	—	0.006	—	0.02
—	—	—	—	—	—	—
0.0001	—	—	0.002	0.005	0.0001	0.03
0.0006	—	—	0.002	—	0.0001	0.003

integer the result of the following formula: $[(mm \times 24)/100] + 0.5$.

Means were calculated for morning ratings and evening ratings. Total mood variability over the 2-week period was reflected by the standard deviations of the morning and evening ratings. Day-to-day variability was quantified by taking the mean absolute value of the change from one day to the next in morning and evening ratings. Variability within each day was quantified as the mean absolute value of the difference between the morning and evening ratings for each day and the mean positive or negative difference between morning and evening ratings (diurnal variation).

To further assess the character of the morning-to-morning mood variability, one can ask how closely each subject's observed morning-to-morning variability matched the morning-to-morning variability that would be predicted if each morning's mood were to occur randomly within the overall range of moods observed in that subject over the 2 weeks—that is, if each morning's mood were independent of the previous morning's mood. The predicted random morning-to-morning variability for each subject was equal to 1.128 times the standard deviation of the morning rating (the moment constant of the range for $N=2$ observations) (9). We termed the ratio of the observed morning-to-morning variability to the predicted random morning-to-morning variability the random variability ratio. A random variability ratio value of 1.00 suggests that morning moods occurred entirely randomly within that individual's observed range of mood ratings; lower values suggest that each day's mood was closer to the previous day's mood rating than the random variability assumption would predict.

An alternative measure of the degree to which one day's rating was associated with the following day's rating can be obtained by calculating, across each subject's series of morning ratings, the autocorrelation with a lag of one day, using the Statistical Analysis Sys-

tem autoregression procedure (10). Higher autocorrelation values represent less random morning-to-morning variation.

Because the distributions of several measures were not normally distributed within the diagnostic groups, non-parametric analyses were used throughout. Kruskal-Wallis one-way analysis of variance by ranks was used for the initial analyses across all groups. When the Kruskal-Wallis test was significant, the Wilcoxon-Mann-Whitney test was applied to pairwise comparisons between groups; the level of significance was set at $p < 0.05$.

Because the standard 100-mm line visual analog scale and the 24-circle adaptation of the visual analog scale for optical scanning have not previously been shown to be comparable, a preliminary analysis was performed comparing the ratings of the eight normal individuals who completed the standard 100-mm line with those of the 16 normal individuals who used the optical scanning version. No significant differences were found on any of the measures of mood or mood variability.

RESULTS

The mean values for the four diagnostic groups are given in table 1. On each of the ratings except diurnal variation, the four groups were significantly different according to Kruskal-Wallis one-way analysis of variance by ranks. Pairwise comparisons using Wilcoxon matched-pairs signed ranks test revealed patterns that confirmed our initial hypotheses. On morning and evening ratings, the patients with major depression had the lowest mean ratings. These ratings were significantly lower than those of the patients with borderline personality disorder, which in turn were significantly lower than those of the patients with PMS and the normal comparison subjects. The latter two groups were not significantly different on morning and evening ratings.

Total variability over the 2-week period as measured by the mean standard deviations of the morning and evening ratings was lowest in the patients with major depression. The variability in the patients with major depression was significantly lower than that in the patients with borderline personality disorder and the normal comparison subjects. The latter two groups were not significantly different from each other. The highest total variability was observed in the group with PMS. The values for the standard deviations of the morning and evening ratings for these patients were significantly higher than those for the other three groups.

Day-to-day variability was measured by the mean absolute value of the differences from one morning to the next and from one evening to the next. The patients with major depression and the normal comparison subjects had significantly lower differences from one morning to the next than did the patients with borderline personality disorder and those with PMS. Ratings of the differences from one evening to the next showed fewer diagnostic differences among the four groups; only the patients with major depression had values that were significantly lower than those of the patients with borderline personality disorder and PMS.

Variability within each day was measured by the mean absolute difference between morning and evening self-ratings. This value was significantly lower for the patients with major depression than for all of the other groups. The value for the patients with borderline personality disorder was significantly higher than those for both the patients with major depression and the normal comparison subjects.

The absolute differences between morning and evening values are not measures of classical diurnal variation because they assess absolute change rather than the direction of change. Mean diurnal variation, a measure that does assess the direction of change, was not significantly different from zero in any group, and there were no significant differences between groups.

The random variability ratio was most distinctive in the two groups with the greatest variability. The random variability ratio for the patients with PMS was significantly lower than that for any other group. The random variability ratio for the patients with borderline personality disorder was significantly higher than that for the patients with PMS or those with major depression.

The degree of autocorrelation with a lag of one day within each individual's morning ratings was significantly higher for the patients with PMS than for any other group.

To summarize by diagnostic group, the patients with major depression had the lowest mean morning and evening ratings, indicating the lowest general mood. Variability of mood in the patients with major depression was also low, reflected by low standard deviations of the morning and evening ratings, low morning-to-morning variability, low evening-to-evening variability, small differences between morning and evening, and low diurnal variation (indicating the absence of classical diurnal variation). The patients

with borderline personality disorder had morning and evening ratings that were significantly lower than those of the patients with PMS and the normal comparison subjects but significantly higher than those of the patients with major depression. The patients with borderline personality disorder showed higher than normal morning-to-morning variability and higher than normal variability during the course of a day. When patients with borderline personality disorder with ($N=10$) and without ($N=6$) a previous history of major depression were compared, no significant differences were observed on any of the measures of mood or mood variability. The patients with PMS had mean mood ratings that were indistinguishable from those of the normal comparison subjects but showed greater mood variability over the 2 weeks. Although the morning-to-morning mood variability in patients with PMS was also higher than normal, these patients had the lowest random variability ratio and the highest mean autocorrelation, indicating that, within the range of variability observed for each individual, each morning's mood rating was more closely associated with the previous day's rating in patients with PMS than in the other diagnostic groups.

To illustrate the typical pattern of mood self-ratings in each diagnostic group, we selected the individual in each group whose ratings most closely matched the group's mean, standard deviation, and morning-to-morning variability and graphed their self-ratings in figure 1.

DISCUSSION

Global visual analog scale ratings of morning and evening mood over a 2-week medication-free period distinguished four diagnostic groups from each other. The three groups of psychiatric patients and the group of normal comparison subjects differed on measures of overall mood, overall variability of mood, and day-to-day changes in mood as well as in absolute changes in mood during the course of a single day.

Each of the three psychiatric disorders is marked clinically by prominent depressive symptoms. As expected, the patients with major depression had low global mood ratings and marked stability of those ratings. The patients with borderline personality disorder also had clear signs of depressed mood, but the depressed mood differed from that seen in the patients with major depression in four distinct ways. First, the overall mood in patients with borderline personality disorder was significantly higher than that of the patients with major depression, although still significantly lower than those of the normal individuals and the patients with PMS. Second, mood in the patients with borderline personality disorder was much more variable over the 2-week period than that in the group with major depression. Third, the day-to-day and morning-to-evening mood changes in patients with borderline personality disorder were much greater than those in the patients with major depression. Finally, morning-to-

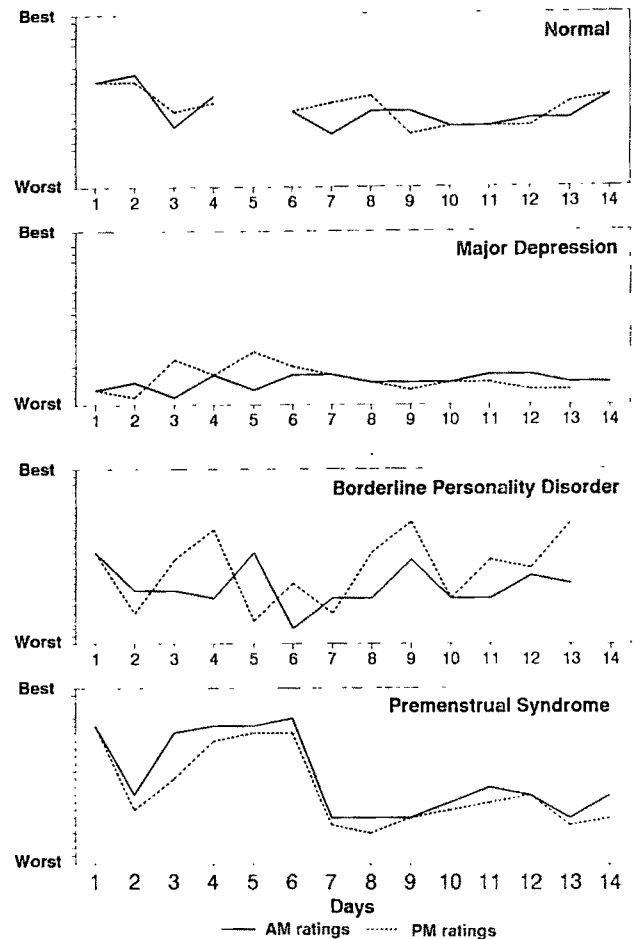
morning changes in mood ratings in the patients with borderline personality disorder showed a more nearly random pattern, as indicated by the high mean random variability ratio of 0.94 and the low mean autocorrelation of $r=0.01$. The random variability ratio approaching 1.0 and the autocorrelation approaching 0.0 suggest that each morning's mood bore almost no relationship to the previous morning's mood in the patients with borderline personality disorder.

Ratings of variability were also high in the patients with PMS, whose overall mean global mood ratings were not significantly different from those of the normal comparison subjects. What distinguished the mood variability of the patients with PMS from the patients with borderline personality disorder, however, was the lower random variability ratio value and the higher degree of autocorrelation in the patients with PMS. Although the total variability was very high in the patients with PMS, less of the observed total variability was attributable to day-to-day fluctuations than in any other group (random variability ratio=0.62), consistent with a primary mood cycle length of roughly 28 days, i.e., much longer than 24 hours.

One additional finding in our study was the relative absence of diurnal variation (worse in morning) in all groups. Although a slight, statistically nonsignificant diurnal pattern was seen in the depressed patients, a comparable nonsignificant degree of diurnal variation was also seen in the normal comparison subjects and in the patients with borderline personality disorder. The patients with PMS showed a slight, nonsignificant reverse diurnal variation (worse in evening). Previous studies of diurnal variation in normal subjects have reported both positive (11, 12) and negative (13) findings, and there is some evidence that diurnal variation is more likely to occur in younger than in older normal subjects (14, 15).

In our sample, diurnal variation did not characterize the patients with major depression. Since the available clinical data did not permit a reliable assessment of melancholia (one criterion of which is diurnal variation), we cannot determine whether diurnal variation occurred specifically in those depressed patients with other indications of melancholia. Other studies have also found that diurnal variation is not a consistent finding in major depression (2, 16, 17) or in melancholia (1-4). When present, diurnal variation does not appear to correlate with severity of depression (3, 12, 18, 19). This form of mood variability requires further study. First, we need to determine whether available instruments such as the visual analog scale are sufficiently sensitive to detect diurnal variation specifically in those individuals who report it in clinical interviews. Second, if the instruments can detect and quantify diurnal variation, we need to determine whether significant diurnal variation is, in fact, characteristic of melancholia and/or other psychiatric disorders, perhaps using the methodology of Carpenter et al. (2), omitting diurnal variation from the criteria for establishing the diagnosis.

FIGURE 1. Visual Analog Scale Mood Self-Ratings Over 14 Days for the Four Patients Whose Morning Ratings Most Closely Matched Morning Mean, Morning SD, and Morning-to-Morning Change for Each Diagnostic Group



Methodological Issues

Possible biases in subject selection require some comment, particularly in studies originating from a research setting in which referral and screening procedures produce relatively homogeneous diagnostic populations, often with more severe or treatment-refractory (and, therefore, possibly atypical) illnesses. The collection of visual analog scale data in a systematic manner across a variety of diagnostic groups in a primary treatment setting would help establish that these different patterns of mood variability are indeed typical of these illnesses. Nonetheless, our confidence in these results is increased by the close correspondence between the empirically observed patterns of mood regulation and the patterns expected on the basis of clinical descriptions of the illnesses.

Scales such as the visual analog scale are extremely simple measures of a complex phenomenon and may be simultaneously characterized as both elegant and crude. Several methodological problems associated with the visual analog scale and with mood ratings in general should be noted. When totally personalized global an-

chors are used (e.g., "worst I've ever felt"), different aspects of positive or negative mood may be emphasized by different individuals in making global judgments, raising questions about the meaning of not only the extreme anchor points but also the unanchored intermediate points on the scale. The global and personalized nature of the scale somewhat compromises its use as a quantitative measure *across* individuals, although all self-rating scales are subject to this criticism to a greater or lesser degree.

The use of the visual analog scale to measure change also poses methodological problems. For example, it is unclear whether an identical 10-mm change in mood rating is comparable across individuals. Furthermore, since all mood rating scales are ordinal rather than interval scales, it is unclear whether a 10-mm increase from 10 mm to 20 mm is equivalent to a 10-mm increase from 50 mm to 60 mm.

Scales are also prone to limit effects. Thus, the variability of mood ratings at the extremes of the scale may be constrained by the lower or upper limit. For example, the only subject with no mood variability had a major depression and rated herself as "worst I've ever felt" every morning of the rating period, posing the question of whether this represented genuinely invariant mood or a limit effect.

Having noted these methodological problems, we feel that several comments are in order. First, the visual analog scale has generally proven to be a particularly sensitive instrument for identifying changes in mood state (13, 20–22). Second, although limit effects may be relevant to the patients with major depression, they do not apply to the other three diagnostic groups, which differed from one another on a number of measures of variability. Third, even if limit effects were present in some cases, the use of the random variability ratio or measures of autocorrelation corrects for the total observed variability within each individual. The existence of group differences in the random variability ratio suggests the likely existence of different *patterns* of variability in addition to the documented differences in the *degree* of variability. Finally, even if cognitive styles contribute to an exaggerated variability in the patients with borderline personality disorder and, possibly, the patients with PMS, cognitive styles are a component of the subjective experience of mood. In other words, mood is inherently a subjective experience, and mood variability is also inherently a subjective phenomenon.

Alternative Approaches to the Study of Mood Variability

These naturalistic studies represent one investigative approach to mood variability. An alternative approach, used most prominently in neuroendocrine research, is the challenge paradigm. This approach is illustrated in an intriguing report of the response of psychiatric patients to two very different sound recordings (23). In this study, patients meeting *DSM-III* criteria for borderline personality disorder or RDC for labile person-

ality showed significantly greater mood changes after listening to the recordings than a mixed comparison group including patients with major depression, bipolar disorder, dysthymic disorder, schizophrenia, and other psychotic disorders.

Acute pharmacological challenges, including amphetamine (24), methylphenidate (25), procaine (26, 27), fenfluramine (28), and m-chlorophenylpiperazine (29) have also been employed to examine mood variability in borderline personality disorder. Such studies using agents with varying pharmacological effects may help determine whether specific neurotransmitter systems are involved in regulating mood variability in borderline personality disorder or whether patients with borderline personality disorder show prominent mood changes in response to any stressor, be it pharmacological, intrapsychic, or environmental.

CONCLUSIONS

Are these results merely adumbrations of the obvious? In one sense, yes. Both major depression and borderline personality disorder are characterized by prominent depressive symptoms, and patients with these disorders have lower global mood ratings than normal comparison subjects and patients with PMS. However, the processes regulating mood in these two "depressed" groups appear to have fundamental differences. Compared with normal subjects, depressed patients have a pathologically stable mood, whereas patients with borderline personality disorder (and those with PMS) have a pathologically unstable mood. These results demonstrate that the usual "depression" of borderline personality disorder may be fundamentally different than the usual "depression" of major depression, a hypothesis supported by research suggesting different pharmacological response profiles for patients with these two disorders (30–32).

For the researcher, the results have additional implications. First, techniques for documenting and investigating "stable-state" phenomena such as major depression may not be particularly applicable to "variable-state" phenomena such as borderline personality disorder. Second, the biological and psychological mechanisms regulating mood may be fundamentally different in major depression, borderline personality disorder, and PMS, although each may produce depressive symptoms. Finally, the mechanisms that regulate overall mood state may differ from those regulating mood stability. In cybernetic terms, one mechanism may regulate the setpoint of the thermostat, while another mechanism may regulate the range of fluctuation around the setpoint. Mood in patients with major depression and in normal subjects may be tightly regulated (well buffered), resulting in a stable mood state, while mood in patients with borderline personality disorder may be loosely regulated (poorly buffered), resulting in wide mood changes in response to perturbations.

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Follow-Up and Family Study of Anxious Depression

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Objective: The failure of the concept of anxious depression to find its way into DSM-III-R led the authors to conclude that a further report on the occurrence of anxiety symptoms in depressed subjects is indicated. **Method:** The subjects were 327 consecutively evaluated inpatients and outpatients with primary unipolar depressive disorder at five university medical centers participating in the National Institute of Mental Health Collaborative Program on the Psychobiology of Depression—Clinical Studies. The authors restricted their sample selection to patients with primary depressive disorder so that patients with other preexisting psychiatric disorders, especially anxiety disorders, would not contaminate the symptom picture, family studies, or follow-up. They examined six anxiety symptoms and derived a new anxiety summary score to show the effect of anxiety in depression on family data and 5-year outcome. **Results:** Depressed subjects with higher ratings for anxiety took longer to recover. There was also a significant relationship between anxiety in depressed probands and the risk for primary unipolar depressive disorder, but not anxiety disorders or alcoholism, among 832 blindly interviewed first-degree relatives. **Conclusions:** These data confirm the usefulness of subdividing depressed patients according to anxiety symptoms: psychic and somatic symptoms of anxiety, taken together, significantly predict family illness and course. The data also emphasize the wisdom of requiring that generalized anxiety disorder not be diagnosed in the presence of a mood disorder. Clearly, symptoms of anxiety coexist with depression and need to be recognized for the effective treatment of the underlying depressive disorder.

(Am J Psychiatry 1991; 148:1512–1517)

DSM-III and DSM-III-R do not allow clinicians to attach “anxious mood” as a modifying descriptor when diagnosing the depressive syndrome. Nor do they include other features of anxiety in the description of depressive disorders. Nonetheless, clinicians and investigators have long recognized the overlap of anxiety and depressive symptoms.

In 1970 Sir Aubrey Lewis (1) published a review of the ambiguous word “anxiety.” He proposed that in psychiatry the technical term “anxiety” had passed through two main phases: first as a qualifying term for the agitated depression of melancholia, then as a qualifying term for a neurosis in which subjective feelings of alarm were associated with visceral disturbances. From his perspective, the first use of the term had little acceptance out-

side of German psychiatry, so only the second, “anxiety neurosis” as christened by Freud, was examined. This paper, however, concerns the first use of the term.

Contrary to Lewis’ beliefs at the time, rating scales for depression in fact emphasized the prominence of anxiety in depression. From such scales, Overall et al. (2) derived three and Paykel (3) four subtypes of depression, the largest group in each being the anxious/tense subtype. In addition, from these reports, the association between anxious and agitated depression to which Lewis referred was confirmed.

Further review of the literature on anxiety symptoms in depressed patients leads us to conclude that many patients with depression can be described as having “anxious depression.” The following findings emerge.

1. Between 15% and 33% of depressed patients have frank panic attacks (4–10).

2. A far larger proportion have other anxiety symptoms. Symptoms that seem to cluster with anxious depression are agitation, obsessive-compulsive symptoms, anorexia/weight loss, gastrointestinal symptoms, hypochondriasis, depersonalization, and diurnal variation (2, 4, 6, 7, 11–14).

3. Despite anecdotal data from clinical writings implying that anxious depression is milder, almost all

Received July 14, 1989; revisions received June 11, 1990, and May 15, 1991; accepted June 17, 1991. From the NIMH Collaborative Program on the Psychobiology of Depression—Clinical Studies. Address reprint requests to Dr. Clayton, Department of Psychiatry, University of Minnesota, Box 77 UMHC, Minneapolis, MN 55455.

Supported in part by U.S. Public Health Service grant MH-25430 from NIMH.

This manuscript has been reviewed by the Publication Committee of the Collaborative Program and has its endorsement.

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studies that compared anxious with nonanxious depressed patients found the former to be more severely ill at index, as measured by Hamilton rating scales or by an incapacitated or endogenous subtype diagnosis (5, 7).

4. Naturalistic studies with follow-ups found depressed patients with anxiety to be more chronically ill and to have a poorer response to treatment (8, 14). In one treatment study comparing depressed patients with panic and patients with pure depression given either 150 mg or more of imipramine or desipramine or 60 mg or more of phenelzine (10), the group with panic had a significantly poorer response at 6 weeks. In another treatment study with tricyclic antidepressants (15), nonresponders had significantly higher baseline anxiety ratings on the Hamilton Rating Scale for Anxiety. Psychic anxiety and panic attacks also predicted an outcome of suicide in the first year (16, 17).

5. Most studies comparing anxious and nonanxious depressed patients that included family data found no difference in the family histories for primary depressive disorder. Four (7, 8, 14, 18) reported more alcoholism in the families of depressed patients with panic attacks, and two (8, 18) reported more of all types of depressive disorder (primary and secondary) in this group.

The failure of the concept of anxious depression to find its way into *DSM-III-R* despite these findings leads us to conclude that a further report on the occurrence of anxiety symptoms in depressed subjects is indicated. We report on inpatients and outpatients with primary depressive disorder and their naturalistic treatments before and after their inclusion into the study. (We define "primary" explicitly in the Method section of this paper.) We restricted our selection to patients with primary depressive disorder so that patients with other preexisting psychiatric disorders, especially anxiety disorders, would not contaminate the symptom picture, family studies, or follow-up. We examined six anxiety symptoms and derived a new anxiety summary score to show the effect of anxiety in depression on family data and 5-year outcome.

METHOD

The probands are participants in the National Institute of Mental Health Collaborative Program on the Psychobiology of Depression—Clinical Studies. Screening procedures and inclusion and exclusion criteria are described elsewhere (19). This is a naturalistic longitudinal study of affective disorders; treatments were carefully recorded but were not controlled by study design. The patients reported on in this paper are the 327 patients who met Research Diagnostic Criteria (RDC) (20) for both lifetime and current definite primary unipolar depressive disorder at update (at discharge or, for outpatients, 2 months after intake).

"Primary" means that the depression was not antedated by an RDC diagnosis of panic disorder, obsessive-compulsive disorder, phobic disorder, alcoholism, drug abuse, sociopathy, or Briquet's disorder at the

definite or probable level. Further, these patients never met RDC for mania, hypomania, or a schizophrenic or schizoaffective episode in the past or during the index hospitalization (or after 2 months in the study as outpatients). Generalized anxiety disorder, as defined by the RDC, could have been present either as a previous disorder or as a present disorder if it preceded the current episode of depression by more than 2 months; only 15 (4.6%) of our patients had ever met RDC for generalized anxiety disorder, and only four (1.2%) exhibited so-called comorbidity in the index episode.

The Schedule for Affective Disorders and Schizophrenia (SADS) (21), the interview used to characterize probands' episodes, includes six symptoms that are frequently considered to be associated with anxiety states such as phobic disorder, generalized anxiety disorder, panic disorder, and obsessive-compulsive disorder. Each symptom is rated from 1 to 6; 1=not at all, 4=moderate, 5=severe, and 6=extreme. However, panic attacks are rated on a 3-point scale on which 1=not present and 3=definite. The six symptoms examined are 1) worry, brooding, painful preoccupation, and inability to get rid of unpleasant thoughts (may or may not be accompanied by depressive mood), 2) panic attacks (circumscribed periods of intense anxiety with at least two physical symptoms not associated with physical exertion or life-threatening situations), 3) somatic anxiety (one or more physiological concomitants of anxiety other than during a panic attack, including the items listed as associated with panic attacks as well as headaches, stomach cramps, diarrhea, or muscle tension, all scored whether or not the subject has had panic attacks), 4) psychic anxiety (subjective feelings of anxiety, fearfulness, or apprehension, excluding panic attacks, whether or not accompanied by somatic anxiety and whether focused on specific concerns or not), 5) phobia (irrational fear of a specific object, activity, or situation that the subject tends to avoid), 6) obsessions or compulsions (recurrent or persistent ideas, images, feelings, impulses, or movements that generally are accompanied by a sense of subjective compulsion and a desire to resist the event and are usually recognized by the individual as foreign to his or her personality or nature, i.e., "ego alien").

Group comparisons of patients with high versus low anxiety ratings were made in several ways. In looking at the time to recovery from the index episode of illness, log-rank chi-square and Cox proportional hazards models were used (22). In examining the rates of nonanxiety depressive symptoms or risk to relatives as a function of proband anxiety, chi-square was used. When examining risks to relatives controlling for proband age at onset, logistic regression was used (23). All statistical analyses were conducted with the Statistical Analysis System (24).

RESULTS

Two hundred eleven (65%) of the 327 subjects were women, their mean±SD age at intake was 41±16.0 years, 74 (23%) were outpatients, and 126 (39%) were

TABLE 1. Anxiety Symptom Ratings in 327 Patients With Primary Unipolar Depression

Symptom	Moderate Rating		Severe Rating	
	N	%	N	%
Worrying	100	30.6	143	43.7
Panic attacks ^a	—	—	88	26.9
Somatic anxiety ^b	69	21.1	67	20.5
Psychic anxiety ^b	89	27.2	124	37.9
Phobia ^b	35	10.7	16	4.9
Obsessive-compulsive features ^b	11	3.4	5	1.5

^aThe range of ratings was 1–3 (1=not present, 2=probable, and 3=definite); ratings of 2 or 3 were scored as severe.

^bThe range of ratings was 1–6 (1=not at all, 4=moderate, 5=severe, and 6=extreme); ratings of 5 or 6 were scored as severe.

experiencing their first depressive episode. The mean age at first episode of major depressive disorder was 29.7 ± 15.2 . The mean age at first outpatient care for any mental disorder was 30.9 ± 15.3 , and the mean age at first hospitalization (if any) was 34.3 ± 15.7 . One hundred sixty-two (50%) had previously received medications, and 60 (18%) had had ECT for major depressive disorder. To summarize, the subjects represented a mixture of inpatients and outpatients with or without previous episodes who had been identified as having unipolar depressive disorder and were being treated at tertiary care centers.

Table 1 shows the high frequency of the anxiety symptoms in these depressed patients. Worrying occurred at a moderate or severe degree in almost 75% of these patients. Psychic anxiety, somatic anxiety, and panic attacks also occurred in a large number of patients. The frequencies of these symptoms were equal in both sexes except that phobic symptoms were reported by more women. None of these symptoms occurred for a sufficient duration before the onset of depression to qualify as a preexisting diagnosis of anxiety disorder. For instance, 55 patients had panic attacks for less than 6 weeks and 33 had panic attacks for more than 6 weeks but only during the depressive episode.

An unrotated principal components analysis of correlations among the anxiety items was performed to determine how these symptoms sorted together. One component explained much of the variance. (Only one eigenvalue was over 1.0; a scree test [24] indicated that there was only one factor.) On this component, all the items had positive loadings of about the same magnitude. For worrying, the first component was 0.53; for panic attacks it was 0.63, for somatic anxiety, 0.63; for psychic anxiety, 0.66; for phobias, 0.66; and for obsessive-compulsive features, 0.48. The eigenvalue was 2.17. Therefore, we decided to total the anxiety symptoms to yield a single score for each depressed patient, thus using a summary dimensional approach to these symptoms. The range of the anxiety summary score was from 6 (no anxiety symptoms present) to 33 (the highest possible rating on each item) because 1 means "not at all" on the SADS.

For simplicity and as an heuristic approach, we di-

vided patients into those with high (16 or more) ($N=172$) and low (15 or less) ($N=155$) anxiety ratings in all further analyses. This is a split at the median. When we did this and looked at treatment before intake, we found that those depressed patients with high anxiety ratings were significantly more likely to receive psychotherapy (58% [$N=100$] versus 47% [$N=73$]) and antidepressants (69% [$N=119$] versus 57% [$N=88$]). This was true even though there was no difference in the severity of their illnesses as measured by the Global Assessment Scale (GAS), a 100-point scale combining symptom severity with functional impairment. Each group had a median GAS score of 35. In the first 6 months after admission to the study, patients with high anxiety ratings were significantly more likely to be receiving lithium (17% [$N=29$] versus 9% [$N=14$]).

We tested the difference between probands with high and low anxiety ratings on scores for 39 other SADS-assessed symptoms that are diagnostic of or often associated with depression. If one considers a t test with $p < 0.0013$ to be significant (corresponding to an overall type I error rate of 0.05 by Bonferroni correction), then the following symptoms were significantly more intense in highly anxious depressed patients: depressed mood, negative self-evaluation, discouragement, diurnal variation, depersonalization or derealization, somatic overconcern, difficulty concentrating, insomnia, lack of energy, psychomotor agitation, subjectively experienced anger, distrustfulness, and nonreactivity of mood to changes in circumstances. No symptom was significantly more frequent or intense in the low-anxiety group.

Next we examined the relationship among high versus low anxiety, gender, and age. We found no appreciable or statistically significant relationship between either sex or age on the one hand and the anxiety classification on the other.

Blind lifetime version of the SADS (SADS-L) (21) interviews were conducted with 832 first-degree relatives (parents, siblings, children) of the 327 probands. The dichotomized anxiety summary score was considered in relation to psychiatric diagnoses in first-degree relatives. Table 2 indicates that a strong positive association occurred only between proband anxiety status and the risk of unipolar depressive disorder, chiefly primary depressive disorder. Note that almost all of the relatives with major depressive disorder had unipolar depressive disorder. Hence, the test for a relationship between proband anxiety and the risk to relatives for major depressive disorder essentially duplicates that for unipolar major depressive disorder.

The association between anxiety and risk for primary unipolar depressive disorder remained when proband age at onset of major depressive disorder was simultaneously used as a predictor (logistic regression partial $\chi^2=6.52$, $df=1$, $p<0.02$). The association also persisted when the RDC subtype of recurrent unipolar depressive disorder was simultaneously used as a predictor (logistic regression partial $\chi^2=7.28$, $df=1$, $p<0.007$). These facts are important to interpreting the association be-

tween anxiety and familial risk, since familial risk is sometimes positively correlated with both early age at onset and recurrent major depressive disorder in the proband.

Finally, the relationship between anxiety and outcome was examined. We used survival analysis (SAS PROC LIFETEST) for this comparison. Time to recovery was dated from time of entry into the study. The patients with higher anxiety ratings were slower to recover from their index episodes of major depressive disorder (log-rank $\chi^2=6.76$, $df=1$, $p<0.01$). Median recovery time for those with lower anxiety ratings was 13 weeks, compared with 26 weeks for those with higher ratings (estimated by interpolation in Kaplan-Meier curves).

DISCUSSION

These data confirm the usefulness of subdividing depressed patients according to anxiety symptoms: psychic and somatic symptoms of anxiety, taken together, significantly predict family illness and course. Inpatients and outpatients with primary unipolar depressive disorder who have higher anxiety ratings define a subgroup of patients who have a higher familial prevalence of unipolar primary depressive disorder and a poorer 5-year outcome. They do not have higher familial rates of any of the RDC anxiety disorders or RDC alcoholism, drug abuse, secondary depressive disorder, or bipolar disorders.

The additional symptoms that highly anxious depressed patients are more likely to exhibit are negative self-evaluation, discouragement, more depressed mood, diurnal variation with mood worse in the morning, somatic overconcern (including gastrointestinal symptoms), lack of energy, insomnia, agitation, less ability to concentrate, depersonalization and derealization, subjective anger, distrustfulness, and lack of reactivity of mood to changes in circumstances. These symptoms are similar to those described by Hamilton (11), Rassaby and Paykel (12), Overall and Rhoades (13), VanValkenburg et al. (6, 14), and Garvey et al. (7). Symptoms that are essentially uncorrelated with anxiety score are retardation, a distinct quality to the depressed mood, weight loss, suicidal tendencies, delusions, hallucinations, and bizarre behavior. Thus, this identifies a group of worried, anxious patients rather than a retarded or psychotic group. Kettering et al. (25), in following up delusional depressed patients, also identified a second group of nondelusional, anxious depressed patients.

To illustrate this further, the frequencies of all depressive symptoms in the patients with primary unipolar depressive disorder were examined. Of the 10 most common symptoms (depressed mood, discouragement, loss of interest, trouble concentrating, fatigue, insomnia, worry, negative self-evaluation, social withdrawal, and psychic anxiety), two are anxiety symptoms. These, unlike the others, are not symptoms used to make the diagnosis. This is consistent with the position taken by

TABLE 2. Affective Disorder and Anxiety Disorder Diagnoses in Relatives of 327 Depressed Proband With Low or High Anxiety Ratings

Diagnosis	Relatives of 155 Proband With Anxiety Scores ≤ 15 (N=413)		Relatives of 172 Proband With Anxiety Scores > 15 (N=419)	
	N	%	N	%
Mania	3	0.7	2	0.5
Major depressive disorder ^a	118	28.6	153	36.5
Unipolar depressive disorder ^b	106	25.7	142	33.9
Primary depressive disorder ^c	86	20.8	121	28.9
Secondary depressive disorder	32	7.8	32	7.6
Alcoholism	51	12.4	58	13.8
Panic disorder	9	2.2	8	1.9
Generalized anxiety disorder	27	6.5	30	7.2
Phobic disorder	11	2.7	15	3.6
Any anxiety disorder ^d	43	10.4	45	10.7

^a $\chi^2=6.72$, $df=1$, $p<0.05$.

^b $\chi^2=5.98$, $df=1$, $p<0.01$.

^c $\chi^2=7.22$, $df=1$, $p<0.005$.

^dIncludes obsessive-compulsive disorder, too rare to examine separately.

Cassidy et al. (4), who in their classic paper on 100 patients with manic-depressive disorder and 50 medically ill control subjects designated the mood change necessary for depression as blue, worried, discouraged, depressed, anxious, low, scared, fearful, angry, afraid, gloomy, hopeless, despondent, not caring, empty, and disgusted. They reported that many anxiety symptoms were significantly more frequent in the depressed patients than the control subjects.

The data also emphasize the wisdom, fortunately exercised in *DSM-III-R*, of requiring that generalized anxiety disorder not be diagnosed in the presence of a mood disorder. Given our data showing high rates of anxious symptoms in depressive disorder without much coexisting RDC generalized anxiety disorder (about 1%), we would conclude that such symptoms frequently represent an anxious aspect of depression rather than comorbidity. The place of anxiety symptoms in the definition of depression will be clarified by further work.

The finding of a higher familial prevalence for depression in anxious depressed patients supports the results and conclusions of Angst (26). Although his sample was small, he found, like Stenstedt (27) and Hopkinson (28), a higher morbid risk among relatives of anxious, agitated depressed patients than among relatives of patients with inhibited endogenous depression. He also found more schizophrenia in these relatives.

The theoretical implications of our family data are unclear. There may be a distinct, anxious depressive subtype with higher familial risk. Coryell et al. (8) reported a higher frequency of total major depression but only a trend for primary major depression in the rela-

tives of depressed patients with panic attacks. This may still be consistent with the hypothesis that there are two types of depression because panic attacks alone would not be expected to be as predictive as would all anxiety symptoms taken together.

Another possibility is that these anxiety symptoms measure a pathoplastic factor. Relatives who, by virtue of genes or a common rearing environment, have higher anxiety ratings may be at higher risk for depression. According to this model, the greater risk of depression in relatives should be gradual and roughly proportional to increasing proband anxiety score. A direct test of this theory would require anxiety ratings for all relatives, even those without histories of major depression, which we unfortunately lack.

These anxious depressed patients did not have higher familial rates of other anxiety disorders or alcoholism. The former is consistent with the bulk of the literature but contradicts reports derived from a single epidemiologic sample of depressed patients and their families (18, 29). Not finding higher rates of alcoholism in these families is difficult to explain. It may be that panic attacks (but not more general anxiety symptom scores) in depression (7, 8, 14, 18) predict that association. This needs further study.

These findings also have clinical implications. The patients with higher levels of anxiety were treated with more psychotherapy and antidepressants before entry into the study than were those with lower levels. During the initial phase of the study, they received significantly more lithium. These treatments probably reflect the treatment-resistant nature of anxious depression, also confirmed by the fact that at follow-up they were less likely to have recovered than were their less anxious counterparts. The treatment cannot be related to the presence of psychotic symptoms because those symptoms negatively correlated with high anxiety. The poor outcome is also reflected in the additional finding from the Collaborative Program study (16, 17) that anxiety in the index episode correlated with completed suicide in the first year. It may be that, as Fawcett and Kravitz (5) postulated, if anxiety symptoms are not attended to early in the treatment of the depression, the rates of noncompliance and premature termination may be higher. Or the best treatment has not yet been devised. Both adequacy of antidepressant treatment and compliance need to be reviewed. The presence of anxiety symptoms in depression represents an aspect of drug and ECT trials that needs to be considered. Clearly, anxiety symptoms coexist in depression and need to be recognized for the effective treatment of the underlying depressive disorder.

ACKNOWLEDGMENTS

The NIMH Collaborative Program on the Psychobiology of Depression—Clinical Studies was conducted with the participation of the following investigators: G.L. Klerman, M.D., Chairperson, New York, N.Y.; R.M.A. Hirschfeld, M.D., Co-Chairperson, Washington, D.C.; M.B. Keller, M.D., and P. Lavori, Ph.D., Boston; J.A. Fawcett, M.D., and W.A. Scheftner, M.D., Chicago; W. Coryell, M.D., N.C.

Andreasen, M.D., J. Haley, and P. Wasek, B.A., Iowa City; J. Endicott, Ph.D., and J.E. Loth, M.S.W., New York, N.Y.; J. Rice, Ph.D., and T. Reich, M.D., St. Louis. Other contributors include P.J. Clayton, M.D., J. Croughan, M.D., M.M. Katz, Ph.D., E. Robins, M.D., R.W. Shapiro, M.D., R.L. Spitzer, M.D., and George Winokur, M.D.

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Serotonin Function and Depression: Neuroendocrine and Mood Responses to Intravenous L-Tryptophan in Depressed Patients and Healthy Comparison Subjects

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Objective: This study was designed to compare central serotonergic function in depressed patients and healthy comparison subjects by examining neuroendocrine and mood responses to intravenous L-tryptophan. **Method:** One hundred twenty-six drug-free patients with DSM-III-R major depression (109 unipolar, 17 bipolar; 68 melancholic, 58 nonmelancholic; 28 psychotic, and 98 nonpsychotic patients) and 58 healthy comparison subjects participated. After an overnight fast, subjects received an intravenous infusion of L-tryptophan, 7 g. Blood was obtained for determination of serum prolactin, serum growth hormone (GH), and plasma tryptophan levels. Visual analogue scales were used to assess mood. **Results:** Prolactin responses were blunted in nonmelancholic and higher in melancholic and psychotic depressed patients, while GH responses were blunted in combined unipolar, nonmelancholic, and nonpsychotic depressed patients. Controlling for baseline biological, clinical, and demographic factors eliminated the higher prolactin response in the melancholic and psychotic patients, attenuated the blunted GH response in the unipolar patients, and revealed a blunted GH response in the melancholic patients. Patients and comparison subjects differed on five of 13 mood responses, primarily because of baseline differences. **Conclusions:** These findings are consistent with previous studies demonstrating blunted neuroendocrine responses to intravenous L-tryptophan in depression. Restriction of these findings to specific subtypes of depression may reflect a differential role of serotonergic abnormalities in these subtypes.

(Am J Psychiatry 1991; 148:1518-1525)

Since 1984, there has been increasing use of the pharmacological challenge paradigm to examine the role of serotonin (5-HT) function in the pathogenesis of depression (1). This approach depends on the ability of agents with major effects on 5-HT function to reliably elicit specific neuroendocrine responses. Such responses are taken to reflect the functional status of central 5-HT systems. While discordant findings have been reported, most studies have demonstrated differential responses between depressed patients and healthy control subjects

that are consistent with abnormal 5-HT function in the patients.

Of the many available 5-HT agonists and antagonists (1), published reports to date have used the 5-HT precursors L-tryptophan (2) and 5-hydroxytryptophan (3), the 5-HT releaser fenfluramine (4), the 5-HT reuptake inhibitor clomipramine (5), the mixed 5-HT receptor agonist m-chlorophenylpiperazine (6), and the 5-HT_{1A} agonist gepirone (7). A particularly extensive preclinical literature supports the validity of intravenous L-tryptophan as a probe of central 5-HT function (2). Another advantage of this agent is that its lack of pharmacokinetic interactions with most psychotropic drugs permits its use in assessing drug effects on 5-HT function (2). This has been especially useful in elucidating the clinical neuropharmacology of thymoleptics (2).

Four previous studies have compared the neuroendocrine responses of depressed patients and healthy control subjects to intravenous L-tryptophan. Heninger et al. (8) first reported lower prolactin responses in 24 predominantly nonmelancholic depressed patients than in 19 age- and sex-matched control subjects. Koyama and Meltzer (9) described lower prolactin and growth hormone (GH)

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Supported in part by NIMH grants MH-25642, MH-30929, MH-36229, and MH-00579 and by the Department of Mental Health, State of Connecticut.

The clinical and research staffs of the Ribicoff Research Facilities provided assistance. Huan Gao, M.S., and Sally Trufan assisted in the data analysis.

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TABLE 1. Demographic and Clinical Data for Healthy Comparison Subjects and Depressed Patients, by Diagnostic Subtype

Group	Age (years)		Sex		Weight (lb)		Inpatient/Outpatient		Hamilton Depression Score (25 items)		Hamilton Anxiety Score (14 items)		Short Clinical Rating Scale Score ^a	
	Mean	SD	M	F	Mean	SD	In-patient	Out-patient	Mean	SD	Mean	SD	Mean	SD
Comparison subjects (N=58)	38	13	17	41	152	35	—	—	—	—	—	—	—	—
All major depressed (N=126)	43 ^b	14	38	88	151	36	77	49	33	10	19	7	7	2
Unipolar (N=109)	44 ^c	14	31	78	152	38	63	46	34	11	19	7	7	2
Bipolar (N=17)	40	15	7	10	146	23	14	3	30	7	17	6	7	1
Melancholic (N=68)	47 ^d	15	21	47	145	32	51	17	36	10	20	6	8	1
Nonmelancholic (N=58)	38	10	17	41	159	40	26	32	30	10	17	7	7	1
Psychotic (N=28)	45 ^e	15	6	22	148	40	26	2	40	10	20	6	8	2
Nonpsychotic (N=98)	43 ^f	13	32	66	152	36	51	47	31	10	18	7	7	1

^a1=none, 15=severe.^bt=2.6, df=182, p<0.02. All comparisons are between depression subtype group and comparison subjects.^ct=2.8, df=165, p<0.007.^dt=3.8, df=124, p<0.0002.^et=2.2, df=84, p<0.03.^ft=2.3, df=154, p<0.03.

responses in 20 depressed patients than in 11 control subjects, but suggested that this could have resulted from the lower levels of plasma tryptophan they observed in the depressed patients following intravenous L-tryptophan infusion. Cowen and Charig (10), in a study of 30 depressed patients and 30 control subjects, found that prolactin and GH responses were lower in the patients after the study controlled for weight loss of more than 10 lb, which actually increased the neuroendocrine responses. These authors observed no difference between patients and control subjects in postinfusion levels of plasma tryptophan. Most recently, Deakin et al. (11) reported that GH responses were blunted in 23 depressed patients compared with 22 control subjects, while prolactin responses were attenuated only in patients without weight loss of more than 3 kg. These investigators also found that pre-infusion plasma tryptophan levels were lower and postinfusion tryptophan clearance was more rapid in the depressed patients, although these differences did not appear to account for the neuroendocrine findings.

In the present study of intravenous L-tryptophan, we have attempted to resolve some of these disparities by using a sufficiently large patient sample to permit meaningful comparisons between depressed patients categorized on three major diagnostic dimensions (polarity, melancholia, and psychosis) and comparison subjects. In addition, we present here the first systematic comparison of the acute subjective mood effects of intravenous L-tryptophan in depressed patients and comparison subjects.

METHOD

Subjects

A total of 126 depressed patients and 58 healthy comparison subjects participated in the study after giving

voluntary informed consent. The study was conducted at the clinical neuroscience research unit of a mental health center. None of the patients in the present study was included in the earlier report from our group (8). All subjects were determined to be free of serious medical illness on the basis of a complete physical and neurological evaluation, including ECG and comprehensive laboratory tests of blood and urine.

Patient diagnoses were made by our consensus on the basis of assessments by the treating psychiatrist, nurses' observations, family evaluation, medical records, interview with the Yale Depression Inventory (12), and direct unstructured interview. All patients met *DSM-III-R* criteria for major depression both before and after a minimum 2-week period of placebo antidepressant treatment. *DSM-III-R* criteria were also used to categorize patients by diagnostic subtype (see table 1).

Severity of depressive and anxiety symptoms was assessed at least weekly by a trained research nurse using a 25-item modified Hamilton Rating Scale for Depression and the 14-item Hamilton Rating Scale for Anxiety. The last ratings obtained before the L-tryptophan test day were used for analysis. Inpatients were also rated twice daily by trained nurses using the Short Clinical Rating Scale (13); mean ratings on the global depression item of this scale for the 3 days before the L-tryptophan test day were used for analysis. Ratings of suicidality and weight loss during the current depressive episode were derived from the appropriate items of the Hamilton depression scale.

Peak postdexamethasone plasma cortisol levels were determined in 69 patients on the basis of 4:00 p.m. and 11:00 p.m. levels after administration of dexamethasone, 1 mg p.o., given the preceding night at 11:00 p.m. (outpatients were sampled only at 4:00 p.m.). Sedative/hypnotic use within 24 hours before the L-tryptophan test was ascertained in a randomly

selected subgroup of 42 patients (23 who had used them and 19 who had not) in order to assess any possible effects on neuroendocrine responses (14).

Healthy comparison subjects were obtained by newspaper advertisements and by referral from other healthy volunteers. In addition to the medical screening described earlier, they were also screened for a personal and family (first-degree relative) history of mental disorder by a research psychiatrist using a semistructured interview. Comparison subjects were paid for their participation.

Detailed demographic and clinical data for all subjects, by *DSM-III-R* diagnostic subtype, are presented in table 1.

Procedure

Patients were studied during a placebo period before a blind antidepressant drug trial. At the time of testing, patients had been receiving placebo for at least 2 weeks and had been free of psychotropic drugs (except for low-dose benzodiazepines for severe agitation and insomnia) for at least 3 weeks. Healthy comparison subjects were unmedicated and also agreed to refrain from alcohol use for at least 2 weeks and other psychoactive drug use for at least 4 weeks before testing.

Subjects fasted overnight and throughout the 3-hour test, which began at 9 a.m. in a specially designated challenge room. The test dose consisted of L-tryptophan, 7 g i.v., infused over a 20-minute period. Subjects were awake and in a supine position with head elevated during the procedure. Blood samples for determination of prolactin and GH levels were collected through an indwelling intravenous catheter kept patent by a slow saline drip. Sampling began at least 1 hour after catheter insertion, at 15 minutes before (baseline) and 30, 40, 50, 60, 70, and 90 minutes after the start of the L-tryptophan infusion. Visual analogue scales (0 mm="not at all," 100 mm="most ever") on 13 different mood states (talkative, happy, drowsy, nervous, sad, calm, depressed, anxious, energetic, fearful, mellow, high, and angry) were scored by the patients at these times (omitting the 70-minute time point). At the same times, while the patients were in a sitting position, pulse and blood pressure were measured with a sphygmomanometer in the usual clinical fashion. Blood samples for determination of plasma tryptophan levels were obtained at -15, 30, and 90 minutes.

Biochemical Methods

The L-tryptophan infusions were prepared by dissolving 8.4 g of L-tryptophan in 600 ml of 0.45% saline solution, with 50% sodium hydroxide added to bring the solution to a pH level of 7.4. Each 600-ml aliquot was sterilized by passage through a 0.22-mm filter (Millipore) and was tested for pyrogenicity and sterility before use. Serum samples were assayed for

prolactin levels with a radioimmunoassay kit (Serono Diagnostics, Inc.), with intra-assay and interassay coefficients of variation of 3% and 7%, respectively. GH was assayed with a homologous double-antibody method by using materials provided by the National Institute of Allergy, Metabolic, and Digestive Diseases; intra-assay and interassay coefficients of variation were 5% and 7%. Postdexamethasone plasma cortisol levels were determined with a fluorometric assay (intra-assay and interassay coefficients of 3% and 8%) previously shown to be related to neurobiologic and clinical measures in depressed patients (15). Total plasma tryptophan concentration was measured in 35 patients and 28 comparison subjects by high performance liquid chromatography.

Data Analysis

Because of nonnormal distributions, endocrine data were log₁₀-transformed before analysis (geometric means are presented to facilitate comparison with other studies). Peak change (Δ) in prolactin and GH levels after L-tryptophan administration was calculated by subtracting the baseline from the highest value after L-tryptophan administration. Area under the curve was calculated for neuroendocrine responses and for increases in plasma tryptophan levels after L-tryptophan infusion by using the trapezoidal rule, with baseline levels subtracted from the total. Because neuroendocrine peak Δ and area under the curve responses correlated highly (Spearman's $\rho=0.98$ for prolactin and 0.98 for GH), only peak Δ responses are reported. Subjects with baseline GH levels higher than 5 ng/ml were excluded from analysis.

Differences between the combined depressed group and comparison subjects were assessed with *t* tests. Preliminary analyses of variance (ANOVAs) were then used to examine differences between depressed patients dichotomously characterized on a major diagnostic dimension (unipolar/bipolar, melancholic/nonmelancholic, and psychotic/nonpsychotic) and comparison subjects. *T* tests were used to examine differences between specific depressed subgroups and comparison subjects if the initial ANOVA was significant. Analysis of covariance (ANCOVA) was performed to control for nondiagnostic factors capable of affecting neuroendocrine responses to L-tryptophan; ANCOVA results are noted if the covariate differed significantly between patients and comparison subjects (see table 1) or if the covariate was significantly correlated with the dependent variable in question. Spearman's ρ was used to evaluate relationships between untransformed endocrine and other variables. To minimize type I error, data were analyzed only for diagnostic groups in which the neuroendocrine response in question differed from that of comparison subjects. Visual analogue scale data were subjected to preliminary ANOVAs, followed by further analysis, as described earlier. All statistical tests were two-tailed, with significance at $p<0.05$.

TABLE 2. Neuroendocrine Responses to Intravenous L-Tryptophan in Healthy Comparison Subjects and Depressed Patients, by Diagnostic Group

Group	Prolactin (ng/ml) ^a				GH (ng/ml) ^a				Plasma Tryptophan			
	Baseline		Peak Δ		Baseline		Peak Δ		Baseline (μg/ml) ^b		Area Under the Curve (mg-min/ml)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Comparison subjects (N=58)	4.0	2.6	3.1	2.0	1.1	2.5	6.9	3.4	7.5	1.7	13.0	2.7
All major depressed (N=126)	3.5	2.2	3.2	2.1	1.2	2.0	4.1 ^c	3.1	7.3	1.6	12.8	2.5
Unipolar (N=109)	4.0	2.3	3.2	2.2	1.2	2.0	4.2 ^d	2.9	7.2	1.7	12.9	2.7
Bipolar (N=17)	3.2	1.7	3.0	1.4	1.1	2.1	3.7	4.5	8.0	1.2	12.1	1.0
Melancholic (N=68)	2.7 ^e	2.3	4.2 ^f	2.0	1.1	2.0	4.6	2.8	7.0	1.6	12.7	2.5
Nonmelancholic (N=58)	4.6	1.9	2.3 ^g	1.9	1.3	1.9	3.6 ^h	3.4	7.7	1.6	12.9	2.7
Psychotic (N=28)	2.6	2.1	4.8 ⁱ	2.2	0.9	2.2	6.1	2.9	6.5	1.7	12.9	3.3
Nonpsychotic (N=98)	3.7	2.2	2.9	2.0	1.3	1.9	3.7 ^j	3.1	7.5	1.6	12.9	2.4

^aProlactin and GH data are presented as geometric means±SD (statistical tests were performed on log₁₀-transformed values).

^bTryptophan levels are presented as means±SD of the raw (untransformed) values.

^ct=2.6, df=158, p<0.01. All comparisons are between depression subtype group and comparison subjects.

^dt=2.5, df=141, p<0.02.

^et=2.5, df=121, p<0.02.

^ft=2.3, df=121, p<0.03.

^gt=2.2, df=111, p<0.03.

^ht=2.6, df=100, p<0.01.

ⁱt=2.6, df=81, p<0.02.

^jt=3.0, df=135, p<0.004.

RESULTS

Subject Characteristics and Tryptophan Levels

Table 1 shows that the combined depressed group was significantly older than the comparison group. The melancholic, unipolar, nonpsychotic, and psychotic groups were also older, whereas the nonmelancholic and bipolar groups did not differ from comparison subjects. Neither combined nor subtyped depressed groups differed significantly from comparison subjects in sex ratio or weight. Baseline and area under the curve tryptophan levels did not differ between depressed patients and comparison subjects (table 2).

Prolactin

Baseline prolactin levels differed significantly among melancholic/nonmelancholic patients and comparison subjects ($F=7.37$, $df=2, 177$, $p<0.0008$). Table 2 shows that baseline prolactin levels were lower in melancholic patients than in comparison subjects; there was no difference between comparison subjects and nonmelancholic patients. Baseline prolactin levels did not differ from comparison subjects in the combined or other depressed groups.

Peak Δ prolactin response after L-tryptophan infusion differed significantly among comparison subjects and melancholic/nonmelancholic patients ($F=11.14$, $df=2, 177$, $p<0.0001$) and psychotic/nonpsychotic patients ($F=5.65$, $df=2, 177$, $p<0.005$). Table 2 shows that peak Δ prolactin was lower in nonmelancholic patients, but higher in melancholic patients, than in comparison subjects. Peak Δ prolactin was higher in psychotic patients than in comparison subjects; there was no difference between comparison subjects and nonpsychotic pa-

tients. Peak Δ prolactin did not differ from comparison subjects in the combined or unipolar/bipolar groups.

ANCOVAs covarying for age failed to alter these findings. Weight and baseline tryptophan levels proved to be statistically significant covariates in ANCOVAs of peak Δ prolactin response involving the combined, unipolar/bipolar, melancholic/nonmelancholic, and psychotic/nonpsychotic groups. Controlling for weight had no effect on differences in peak Δ prolactin response between depressed groups and comparison subjects. However, controlling for baseline tryptophan level eliminated the difference in peak Δ prolactin response between comparison subjects and the melancholic ($F=0.02$, $df=1, 40$, n.s.) and psychotic ($F=0.02$, $df=1, 27$, n.s.) groups. Area under the curve tryptophan levels were not significant covariates.

When baseline prolactin levels and prolactin responses in patients and comparison subjects were compared by sex, nonmelancholic women had a blunted peak Δ prolactin compared with comparison subjects (mean±SD=2.5±2.0 versus 3.4±2.0 ng/ml; $t=2.14$, $df=77$, $p<0.04$). Melancholic women had a higher peak Δ prolactin than comparison subjects (5.0±2.1 versus 3.4±2.0 ng/ml; $t=2.34$, $df=83$, $p<0.03$), and psychotic women had a lower baseline prolactin than comparison subjects (2.6±2.2 versus 4.4±2.6 ng/ml; $t=2.07$, $df=58$, $p<0.05$) and a higher peak Δ prolactin than comparison subjects (5.5±2.1 versus 3.4±2.0 ng/ml; $t=2.47$, $df=58$, $p<0.02$). There were no differences between men in these diagnostic groups and comparison subjects.

Growth Hormone

Baseline GH levels did not differ from comparison subjects in the combined or other depressed groups.

Peak Δ GH response after L-tryptophan infusion differed significantly among comparison subjects and combined depressed patients ($t=2.62$, $df=158$, $p<0.01$), unipolar/bipolar patients ($F=3.51$, $df=2$, 157 , $p<0.04$), melancholic/nonmelancholic patients ($F=3.98$, $df=2$, 157 , $p<0.03$), and psychotic/nonpsychotic patients ($F=5.14$, $df=2$, 177 , $p<0.007$). Table 2 shows that peak Δ GH was lower in combined depressed, unipolar, nonmelancholic, and nonpsychotic patients than in comparison subjects; there were no significant differences between comparison subjects and bipolar, melancholic, and psychotic patients.

ANCOVAs covarying for age reduced the difference in peak Δ GH between unipolar patients and comparison subjects to trend-level significance ($F=3.43$, $df=1$, 140 , $p<0.07$), with no effect on other findings. Weight was a statistically significant covariate in ANCOVAs of peak Δ GH in the combined, unipolar/bipolar, melancholic/nonmelancholic, and psychotic/nonpsychotic groups. Controlling for weight resulted in statistical significance for the blunted peak Δ GH in melancholic patients compared with comparison subjects ($F=4.42$, $df=1$, 104 , $p<0.04$), with no effect on other findings. Baseline tryptophan level was a significant covariate in the ANCOVA of peak Δ GH in the unipolar/bipolar group, reducing the difference in peak Δ GH between unipolar patients and comparison subjects to trend-level significance ($F=3.25$, $df=1$, 47 , $p<0.08$). Area under the curve tryptophan levels were not significant covariates.

When baseline GH levels and GH responses in patients and comparison subjects were compared by sex, nonmelancholic women had a blunted peak Δ GH compared with comparison subjects (3.3 ± 3.2 versus 6.2 ± 3.3 ng/ml; $t=2.11$, $df=68$, $p=0.03$), and nonpsychotic women had a blunted peak Δ GH compared with comparison subjects (3.3 ± 3.0 versus 6.2 ± 3.3 ng/ml; $t=2.46$, $df=89$, $p<0.02$). Differences from the comparison subjects in the combined depressed and unipolar women, and in the combined depressed, unipolar, nonmelancholic, and nonpsychotic men, did not reach significance.

Subjective Mood Effects

Since there was little prior empirical or theoretical basis for expecting differences among diagnostic groups, Bonferroni's adjustment was applied to the preliminary ANOVAs of the visual analogue-rated mood responses to L-tryptophan infusion (adjusted p [p_a]= $39p$). The ANOVAs revealed significant differences among comparison subjects and unipolar/bipolar patients (talkativeness: $F=3.09$, $df=10$, 605 , $p_a<0.03$; happiness: $F=5.41$, $df=10$, 705 , $p_a<0.0004$; energy: $F=4.75$, $df=10$, 715 , $p_a<0.0004$), melancholic/nonmelancholic patients (happiness: $F=5.60$, $df=10$, 705 , $p_a<0.0004$; calmness: $F=3.01$, $df=10$, 700 , $p_a<0.04$; energy: $F=3.67$, $df=10$, 715 , $p_a<0.004$; fear: $F=5.33$, $df=10$, 715 , $p_a<0.004$), and psychotic/nonpsychotic patients (happiness: $F=5.04$, $df=10$, 705 , $p_a<0.0004$; energy: $F=3.78$, $df=10$,

715 , $p_a<0.004$). Figure 1 shows the patterns of responses by diagnostic subgroup for each mood state in which the initial ANOVA was significant. Baseline differences between comparison subjects and patients appear to account for the major findings. There were no significant differences between comparison subjects and patients in ratings of drowsy, nervous, sad, depressed, anxious, mellow, angry, or high feelings.

Relationships Between Neuroendocrine and Other Variables

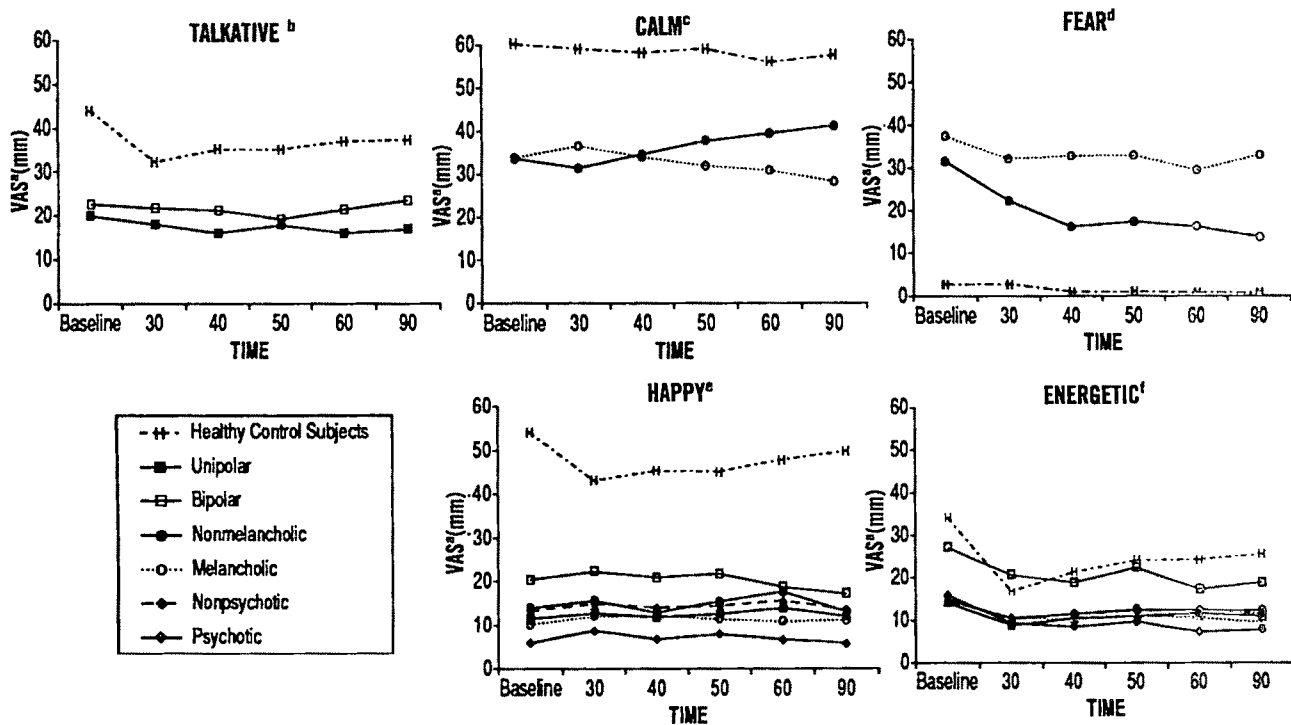
Age was not correlated with peak Δ prolactin in the comparison, nonmelancholic, melancholic, or psychotic groups. Age was negatively correlated with peak Δ GH ($\rho=-0.35$, $df=49$, $p<0.02$) in the comparison subjects but not in the combined, unipolar, nonmelancholic, or nonpsychotic groups.

Weight was negatively correlated with peak Δ prolactin in the comparison ($\rho=-0.66$, $df=55$, $p<0.0001$), nonmelancholic ($\rho=-0.60$, $df=56$, $p<0.0001$), melancholic ($\rho=-0.60$, $df=66$, $p<0.0001$), and psychotic ($\rho=-0.44$, $df=26$, $p<0.04$) groups. Weight was negatively correlated with peak Δ GH in the combined ($\rho=-0.31$, $df=113$, $p<0.0009$), unipolar ($\rho=-0.34$, $df=96$, $p<0.0008$), nonmelancholic ($\rho=-0.39$, $df=52$, $p<0.004$), and nonpsychotic ($\rho=-0.32$, $df=88$, $p<0.004$) groups, but not in the comparison subjects.

Peak Δ prolactin was negatively correlated with baseline tryptophan levels ($\rho=-0.45$, $df=19$, $p<0.05$) and positively correlated with area under the curve tryptophan levels ($\rho=0.45$, $df=19$, $p<0.05$) in the melancholic patients but not with either in the nonmelancholic patients, psychotic patients, or comparison subjects. Peak Δ GH was not correlated with either baseline or area under the curve tryptophan levels in the combined, unipolar, nonmelancholic, nonpsychotic, or comparison groups.

Peak Δ prolactin was positively correlated with total Hamilton depression score in the melancholic patients ($\rho=0.35$, $df=61$, $p<0.005$). Total Hamilton depression, Hamilton anxiety, and Short Clinical Rating Scale global depression scores were otherwise uncorrelated with neuroendocrine responses in all of the depressed groups examined. Suicidality ratings, derived from the Hamilton depression scale, were also not correlated in these groups; comparison of patients with high versus low suicidality was precluded by the absence of patients with current suicidal behavior in this group. Ratings of recent weight loss, derived from the Hamilton depression scale, were similarly not correlated with neuroendocrine responses. Comparison of patients with high (10 lb or more) versus low (less than 10 lb) recent weight loss showed no differences among neuroendocrine responses in any of the diagnostic groups, but only eight patients in the entire study group met criteria for high weight loss.

Peak postdexamethasone cortisol did not correlate with peak Δ prolactin in the nonmelancholic, melancholic, or psychotic groups. However, peak postdexamethasone

FIGURE 1. Subjective Mood Responses Over Time to Intravenous L-Tryptophan in Healthy Comparison Subjects and Depressed Patients, by Diagnostic Subtype

^aVisual analogue scale (0 mm="not at all," 100 mm="most ever").

^bUnipolar, $p < 0.02$; bipolar, $p < 0.04$. All comparisons are ANOVA and are between depression subtype group and comparison subjects.

^cNonmelancholic, $p < 0.02$.

^dNonmelancholic, $p < 0.00001$.

^eUnipolar, $p < 0.00001$; bipolar, $p < 0.0004$; nonmelancholic, $p < 0.0001$; nonpsychotic, $p < 0.00001$; psychotic, $p < 0.0001$.

^fUnipolar, $p < 0.00001$; nonmelancholic, $p < 0.003$; melancholic, $p = 0.00001$; nonpsychotic, $p < 0.00001$.

cortisol was negatively correlated with peak Δ GH in the combined ($\rho = -0.26$, $df = 62$, $p < 0.05$), unipolar ($\rho = -0.35$, $df = 51$, $p < 0.02$), nonmelancholic ($\rho = -0.53$, $df = 22$, $p < 0.01$), and nonpsychotic ($\rho = -0.42$, $df = 49$, $p < 0.003$) groups. Comparison of dexamethasone suppressors (cortisol level of 5 mg/dl or lower) with nonsuppressors (higher than 5 mg/dl) revealed lower peak Δ GH in nonmelancholic nonsuppressors than suppressors (1.5 versus 6.0 ng/ml; $t = 2.14$, $df = 21$, $p < 0.05$); there were no differences in other diagnostic groups.

Peak Δ prolactin was positively correlated with peak Δ GH in the combined ($\rho = 0.33$, $df = 113$, $p < 0.0003$), unipolar ($\rho = 0.32$, $df = 96$, $p < 0.002$), nonmelancholic ($\rho = 0.45$, $df = 52$, $p < 0.0007$), and nonpsychotic ($\rho = 0.40$, $df = 88$, $p < 0.0001$) groups but not in the melancholic patients, psychotic patients, or comparison subjects ($\rho = 0.08$, $df = 47$, n.s.).

Inpatients had higher peak Δ prolactin than outpatients in the combined depressed (3.8 ± 2.0 versus 2.5 ± 2.1 ng/ml; $t = 3.38$, $df = 122$, $p < 0.001$), unipolar (4.0 ± 2.1 versus 2.4 ± 2.1 ng/ml; $t = 3.44$, $df = 105$, $p < 0.0008$), and nonpsychotic (3.4 ± 1.9 versus 2.4 ± 2.0 ng/ml; $t = 2.67$, $df = 95$, $p < 0.009$) depressed groups; there were no differences in other groups. Sedative/hypnotic use had no effect on neuroendocrine responses in any diagnostic groups.

DISCUSSION

This study demonstrated lower prolactin responses to L-tryptophan in nonmelancholic depressed patients; higher prolactin responses in melancholic and psychotic depressed patients; and lower GH responses in combined, unipolar, nonmelancholic, and nonpsychotic depressed patients than in comparison subjects. Controlling for baseline plasma tryptophan eliminated the higher peak Δ prolactin in the melancholic patients and psychotic patients and reduced the significance of the blunted peak Δ GH in the unipolar patients. Controlling for age also diminished the significance of the blunted peak Δ GH in the unipolar patients, but controlling for weight revealed significant blunting of peak Δ GH in the melancholic patients. Findings could not be explained on the basis of changes in plasma tryptophan levels or sex differences among groups, although neuroendocrine differences appeared primarily in women. Age was negatively correlated with GH responses in comparison subjects but not in patients; prolactin and GH responses were unrelated in comparison subjects, melancholic patients, or psychotic patients but positively correlated in the combined, unipolar, nonmelancholic, and nonpsychotic groups. Postdexamethasone cortisol correlated negatively with peak Δ

GH in the combined, unipolar, nonmelancholic, and nonpsychotic groups. However, other clinical variables, including measures of depression, anxiety, suicidality, recent weight loss, inpatient/outpatient status, and sedative/hypnotic use, showed little consistent or meaningful relationship with neuroendocrine responses.

Differences between comparison subjects and depressed patients in subjective mood responses to L-tryptophan seemed to derive from baseline differences between groups. Comparison subjects showed diminution of positive feelings (talkative, happy, energetic), which they rated higher at baseline. In contrast, patients reported diminution of one negative feeling (fearful), which they rated higher at baseline, and enhancement of one positive feeling (calm), which they rated lower at baseline. In light of numerous previous reports that L-tryptophan has some efficacy as an antidepressant treatment, it is notable that depressed patients showed no change in ratings of depressed and sad feelings.

The present observation of blunted prolactin and GH responses in depressed patients generally replicates previous work (8–11) but with some notable differences. The finding of a blunted prolactin response in nonmelancholic patients is consistent with our earlier study (8) but conflicts with the findings of Cowen and Charig (10), who noted blunting primarily in melancholic patients with weight loss of less than 10 lb. Deakin et al. (11) also reported that blunting was only evident in depressed patients without significant weight loss. Although they did not examine the melancholic/nonmelancholic distinction, their report implied that endogenicity (as defined by the Newcastle scale) was unrelated to prolactin response. Koyama and Meltzer (9) did not categorize their patients by diagnostic subtype or weight loss. The higher prolactin responses in the melancholic patients and psychotic patients in the present study may be artifactual, since they are entirely accounted for by differences in baseline plasma tryptophan.

We observed blunted GH responses in combined, unipolar, nonmelancholic, and nonpsychotic patients, and in melancholic patients after covarying for weight. Cowen and Charig (10) found GH blunting only in depressed patients without weight loss, with no difference between melancholic patients and nonmelancholic patients. Deakin et al. (11), observing little effect of weight loss, found significantly greater GH blunting in patients with endogenous depression than in patients with nonendogenous depression. These investigations did not explicitly address the unipolar/bipolar distinction. However, using an L-tryptophan dose of 50 mg/kg, given intravenously in the afternoon, Nurnberger et al. (16) found no evidence of prolactin or GH blunting in remitted bipolar patients compared with control subjects, although cortisol and adrenocorticotrophic hormone responses were attenuated in the patients.

Given the methodological similarities between our study and those of Cowen and Charig (10) and Deakin et al. (11), it seems likely that differences in patient groups contributed significantly to the observed dis-

parities. The majority of our patients were severely depressed, hospitalized, had been receiving treatment before admission to our facility, and had been relatively refractory to that treatment. Despite the severity of their depression, few of our patients reported significant current weight loss, primarily because of intensive nursing and psychosocial management before testing. These features characterized patients in our first sample as well (8). In contrast, patients in the other two studies appear to have been more acutely ill (10,11).

The present findings add to burgeoning evidence that 5-HT function is abnormal in depression. In addition to pharmacological challenge data, support comes from studies of CSF metabolites, platelet 5-HT function, and postmortem brain 5-HT receptors (2). Emerging evidence of specific abnormalities in the availability of tryptophan (17,18), coupled with the observation that tryptophan depletion can induce depressive relapse in antidepressant-remitted patients (19), suggests that presynaptic mechanisms may be involved. Further work is needed to elaborate these findings into a neurobiologically meaningful nosology of depression.

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Low Electrooculographic Ratios in Patients With Seasonal Affective Disorder

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Objective: Changes in retinal sensitivity to light have been hypothesized as etiological in seasonal affective disorder. This study was undertaken to investigate sensitivity to light in seasonal affective disorder using electrooculography (EOG), an objective measure of retinal light response. **Method:** In a mood disorders clinic, 19 depressed, drug-free patients with seasonal affective disorder, diagnosed by DSM-III-R criteria, were compared with 19 age- and sex-matched normal comparison subjects. All subjects had identical EOG testing performed during the winter. EOG (Arden) ratios were calculated from the EOG data. **Results:** According to multivariate analysis of variance, the EOG ratios in the patients with seasonal affective disorder were significantly lower than those of the normal comparison subjects, although there was considerable overlap in EOG ratios between patients and comparison subjects. **Conclusions:** These results suggest that seasonal affective disorder is associated with subtle retinal abnormalities at the level of the photoreceptor/retinal pigment epithelium complex, consistent with subsensitivity to light. A limitation of this study is that the retinal origins of the EOG response are nonspecific and still not completely elucidated.

(Am J Psychiatry 1991; 148:1526-1529)

Seasonal affective disorder, described by Rosenthal et al. in 1984 (1), is a mood disorder characterized by recurrent winter depressions with summer remissions. Several observations have linked the pathophysiology of seasonal affective disorder to environmental light. The prevalence of seasonal affective disorder increases with higher latitude and is correlated with the shorter daily photoperiod in winter (2). Light therapy, consisting of daily sustained exposure to intense bright light, is an effective treatment for seasonal affective disorder (1, 3-5). The mechanism of action of light therapy is mediated through the eyes and presumably the retina (6). For these reasons, the retina is of interest in studying the pathophysiology of seasonal affective disorder. Some investigators have proposed that changes in sensitivity to light may be an etiological mechanism in seasonal affective disorder, although both subsensitivity and supersensitivity to light have been hypothesized (7, 8).

Noninvasive clinical electrophysiological tests can provide indirect assessments of retinal sensitivity to light. One reported study using the threshold of adaptation to the dark as a test suggested that patients with seasonal affective disorder are more sensitive to light perception during the early part of adaptation to the dark than are comparison subjects (9). The adaptation to the dark threshold test, however, is a psychophysical test that involves some subjective response to determine a threshold light perception.

Electrooculography (EOG) is an objective electrophysiological test of retinal function. EOG measures the standing electrical potential across the eye during eye movements (10). This electrical potential increases when the retina is exposed to light. The electrical potential in the light-adapted eye divided by the potential in adaptation to the dark is known as the EOG ratio (or Arden ratio) and is an indirect measure of light-induced retinal change (11).

EOG studies in depression have shown conflicting results. One early study (12) found EOG abnormalities in affective disorder of unspecified seasonality: depressed patients with psychomotor retardation had low EOG ratios and manic patients had high EOG ratios. Methodological problems in that study, such as lack of standardized diagnostic criteria, diagnostic heterogeneity in patient groups, and inadequate matching of comparison subjects, limit the interpretation of the findings. A more recent study (13) found no differences in EOG

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Supported in part by the Canadian Psychiatric Research Foundation and the Zeldowicz Research Award to Dr. Lam.

The authors thank Ms. Arlene Tompkins and Dr. Joseph Mador for their help in this study.

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measures between patients with nonseasonal, unipolar depression and well-matched comparison subjects.

To our knowledge, there are no previous reports of EOG changes in seasonal depression. In the present study, we examined retinal sensitivity to light in seasonal affective disorder by comparing EOG measures in depressed patients with seasonal affective disorder and in carefully matched comparison subjects.

METHOD

This study received ethical approval from the University of British Columbia. Patients were recruited from the Seasonal Mood Clinic at the University Hospital. Comparison subjects were recruited by advertisement and were matched to patients by sex and age. Patients were assessed with an unstructured clinical interview by psychiatrists experienced in the assessment of mood disorders. Patients and comparison subjects were given the Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorders Version (14), by a psychiatrist. This interview guide is composed of a 21-item Hamilton Rating Scale for Depression (15) and an 8-item addendum that rates "atypical" depressive symptoms such as hypersomnia, hyperphagia, weight gain, and carbohydrate craving. Interrater reliability of the structured interview guide is regularly monitored in the research clinic.

Inclusion criteria included *DSM-III-R* criteria for major depressive disorder, recurrent, seasonal pattern, and a score of greater than 15 on the Hamilton Rating Scale for Depression. Comparison subjects were interviewed by a research psychiatrist (R.W.L.) and had no previous history or family history of mood disorder. Exclusion criteria for patients and comparison subjects included a history of cataracts or retinal disease, severe myopia, and psychotropic drug use within the past 4 weeks.

After giving informed consent, all subjects underwent identical EOG protocols at our electrodiagnostic ophthalmology unit. EOGs were done between October and March, with testing times between 9:00 a.m. and 3:00 p.m. Pupils were dilated by using tropicamide 1%, and gold surface electrodes were placed at the lateral and medial canthi of each eye, referenced to each other. All subjects were tested following 25 minutes of adaptation to the dark. Ocular saccades were guided by two light-emitting diodes placed 15 degrees horizontally from a central fixation light-emitting diode located on the surface of a full-field (ganzfeld) stimulator. Recording of saccades was continued for 12 minutes during adaptation to the dark and a further 12 minutes during adaptation to the light. Twenty saccades every 30 seconds were elicited for analysis. The adapting background was a uniform white ganzfeld of surface luminance 202 cd/m². The EOG was recorded on an AC-coupled system with band width 0.1 to 20 Hz. EOG data were recorded digitally and analyzed manually for calculation of voltages in adaptation to the light and the dark and EOG ratios.

The EOG ratio was calculated as the ratio of the maximum potential in adaptation to the light divided by the minimum potential in adaptation to the dark. The data were analyzed by using repeated measures multivariate analysis of variance (MANOVA) with one grouping factor (diagnosis, with two levels: seasonal affective disorder and comparison) and one repeated measure (eye, with two levels: right and left). Data analysis was done on a microcomputer using the SPSS/PC+ statistical package (16).

RESULTS

Nineteen patients and 19 comparison subjects completed the study. Each group consisted of four men and 15 women. All subjects had been free of psychotropic medication for at least 2 months. The mean \pm SD ages of the patients and comparison subjects (36.4 ± 9.4 and 35.4 ± 9.2 years, respectively) were not significantly different ($t=0.33$, $df=36$, $p<0.74$). Seventeen of the patients with seasonal affective disorder had recurrent depressions (unipolar), and two patients had clear hypomanic episodes in the spring and summer (bipolar type II). The mean Hamilton Rating Scale for Depression scores were 20.9 ± 4.5 for patients and 1.1 ± 1.0 for comparison subjects. The mean atypical addendum scores for patients and comparison subjects were 14.0 ± 4.6 and 1.6 ± 1.5 , respectively.

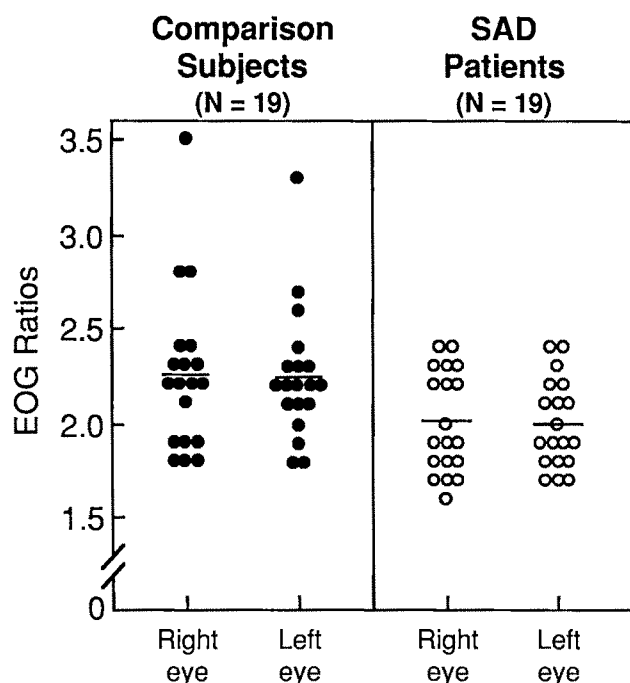
The EOG ratios for each eye are shown in figure 1. The mean EOG ratios for patients were 2.01 ± 0.27 (right eye) and 2.00 ± 0.23 (left eye). The mean EOG ratios for comparison subjects were 2.25 ± 0.42 (right eye) and 2.25 ± 0.34 (left eye). Repeated-measures MANOVA found a significant main effect of diagnosis ($F=5.86$, $df=1$, 36 , $p<0.02$) but not of eye ($F=0.15$, $df=1$, 36 , $p<0.70$). There was no diagnosis-by-eye interaction ($F=0.02$, $df=1$, 36 , $p<0.90$). Inspection of figure 1 suggests a potential outlier in the comparison group that might contribute to the intergroup difference. Reanalysis with this subject excluded did not change the significant effect of diagnosis ($F=4.97$, $df=1$, 35 , $p<0.04$).

In our laboratory, the 95th percentile for EOG ratios for normal subjects is 1.9–3.7, with a median of 2.3 (unpublished data). The EOG ratio is considered borderline between 1.7 and 1.9, and EOG ratios of 1.6 or less are considered abnormal. In the comparison subjects, only nine (24%) of the 38 EOG ratios fell in the borderline range, but 20 (53%) of the 38 EOG ratios in patients with seasonal affective disorder were borderline ($\chi^2=6.75$, $df=1$, $p<0.01$).

DISCUSSION

The results of this study show that EOG ratios are significantly lower in patients with seasonal affective disorder than in matched normal comparison subjects. In clinical use, only low EOG ratios are considered abnormal and indicative of retinal pathology. Only one

FIGURE 1. EOG Ratios for Each Eye in Depressed Patients With Seasonal Affective Disorder (SAD) and Age- and Sex-Matched Normal Comparison Subjects^a



^a Horizontal lines indicate mean values, which differed significantly between groups ($F=5.86$, $df=1, 36$, $p<0.02$).

EOG ratio in the entire series was abnormal—1.6 in a patient with seasonal affective disorder. The other EOG ratios in the patients with seasonal affective disorder fell within an ophthalmological normal or borderline range and were not considered clinically indicative of retinal impairment. Patients were carefully matched to the comparison subjects on the variables that are known to affect the EOG (age and sex), however. A greater proportion of the patients with seasonal affective disorder than the comparison subjects had borderline EOG ratios (53% versus 24%). The EOG changes observed may thus represent a more subtle retinal abnormality in seasonal affective disorder.

The physiological origin of EOG changes is likely within the retinal pigment epithelium (17). The retinal pigment epithelium is intimately associated with rod and cone photoreceptors and is involved in photoreceptor disk renewal mechanisms (18). Subtle retinal changes may be sufficient to affect disk-shedding responses and retinal photostasis (19). Our data are thus consistent with the hypothesis of Reme et al. (7) that seasonal affective disorder is associated with disturbed retinal photoreceptor renewal mechanisms that result in subsensitivity to light. Bright light exposure may then normalize sensitivity to light by enhancement of retinal photoreceptor synthetic activity. Changes in retinal sensitivity to light would also be consistent with the abnormal phase-delayed circadian rhythms in seasonal affective disorder that normalize with light therapy (20, 21).

If patients with seasonal affective disorder have lower sensitivity to light, then the bright light of light therapy may be required to provide the necessary light cue for successful entrainment of circadian rhythms.

Despite the significantly lower mean EOG ratios in the patients, a substantial overlap in EOG ratios was also observed between patients with seasonal affective disorder and comparison subjects. The EOG ratio reflects the change in electrical potential between adaptation to dark and adaptation to light. A lower EOG ratio, therefore, cannot be considered to represent a biological marker or diagnostic test for seasonal affective disorder. It may, however, tell us something about the underlying mechanisms of seasonal affective disorder. The rise in the EOG in response to light is dependent on photoreceptor function as well as intact retinal pigment epithelium function. Thus, we are unable to determine whether the differences in EOG ratios were due to abnormalities in the photoreceptors or in retinal pigment epithelium function. Specific tests of photoreceptor function (for example, electroretinography) will be more helpful in defining these changes in sensitivity to light.

Retinal mechanisms have also been proposed for the etiology of nonseasonal depression, possibly through light-mediated changes in neuroendocrine and/or circadian systems (22). The EOG changes in seasonal affective disorder, however, contrast with the normal EOG findings reported in nonseasonal depressions (13). Other clinical and biological differences between seasonal and nonseasonal depression have been described. In contrast to the "typical" symptoms of melancholia (insomnia with early morning waking, appetite and weight loss, diurnal variation of mood with morning worsening), seasonal affective disorder is commonly associated with "atypical" symptoms of depression, including hypersomnia, appetite and weight gain, and afternoon worsening of mood (1, 23, 24). Some well-studied biological markers of melancholia (such as shortened REM latency and early escape from dexamethasone suppression) are not found in seasonal affective disorder (25). Phase-delayed circadian rhythms are described in seasonal affective disorder, but phase-advance hypotheses have been proposed for melancholia (20, 26). Finally, although light therapy has not been studied extensively in nonseasonal depression, patients with nonseasonal depression do not seem to have the same rapid and robust response to bright light exposure shown by patients with seasonal affective disorder (4, 27). Thus, it is plausible that the pathophysiology of seasonal affective disorder and nonseasonal depression would involve different retinal mechanisms. Further work is required to clarify retinal changes that occur in seasonal affective disorder and nonseasonal depressions as well as the effects of light therapy on retinal sensitivity to light.

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REM Latency and the Recovery From Depression: Getting Over Divorce

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***Objective:** The authors' goal was to address five questions: 1) What is the frequency of early REM sleep in subjects in the process of divorce who meet diagnostic criteria for major depressive disorder? 2) What is the frequency of this sign in subjects in the process of divorce who are not depressed? 3) How often does this sign persist following remission of depressive symptoms? 4) What is the predictive value of early REM sleep among depressed subjects for later adjustment to the process of divorce? and 5) What is the role of a family history of depression or alcoholism in the presence and persistence of early REM sleep? **Method:** Two hundred fourteen volunteers undergoing marital separation were recruited; 70 of these subjects were selected for a 3-night sleep study. Forty of the 70 subjects met criteria for depression and 30 did not; 61 (87%) returned for repeat studies 1 year later. **Results:** Fifteen (38%) of the 40 depressed subjects had short REM latency. Seven of these continued to have short REM latency 1 year later, but none of these met the criteria for depression at that time. A higher proportion of these subjects had made a good adjustment to their new life than did depressed subjects whose initial and follow-up REM latencies fell within the normal range. **Conclusions:** These data suggest that depressed individuals with normal REM latency may need more aggressive treatment intervention.*

(Am J Psychiatry 1991; 148:1530-1535)

The specification in the sleep laboratory of several disturbances characteristic of the sleep of patients with the diagnosis of major depressive disorder has generated considerable research over the past 20 years. This research was reviewed by Reynolds and Kupfer in 1987 (1). These authors set out some of the continuing questions concerning shortened latency to the first REM period of the night, the abnormality that has proven the most robust. These questions revolve around three issues: 1) the sensitivity and specificity of this "marker" to the diagnosis of depression, 2) its stability, or its trait-like behavior versus its state-like behavior (is it found only coincident with an episode or does it continue after the remission of symptoms?), and 3) its predictive value for subsequent episodes.

Reynolds and Kupfer (1) emphasized the need for longitudinal studies to address these questions and to

track the behavior of REM latency in relation to the waxing and waning of depressive symptoms. In addition, Giles et al. (2) have reported concordance for shorter REM latency among family members who share the diagnosis of depression. This suggests that there may be a genetic propensity for depression indicated by the presence of this sleep sign.

As part of a larger longitudinal study of volunteers undergoing marital separation with the intention to divorce, sleep studies were performed close to the time of the marital separation and 1 year later for two groups of subjects. One group was chosen because the subjects met subjective and clinical criteria for depression. Subjects in the other group were matched in age, sex, and number of months separated but were not currently depressed. Data from these two groups can address the issues raised by Reynolds and Kupfer and by Giles et al. in a unique group of unmedicated subjects who were not patients, all of whom were undergoing the same stressful life change.

As a life event, divorce, like the bereavement of loss of a spouse (3) or the experience of being wounded in combat (4), is associated with a high rate of depression that often goes undiagnosed and untreated. This makes it a convenient experiment-in-nature for studying the variables associated with the development of, or resis-

Received July 26, 1990; revisions received Dec. 31, 1990, and April 8, 1991; accepted April 29, 1991. From the Sleep Disorder Service and Research Center, Rush-Presbyterian-St. Luke's Medical Center. Address reprint requests to Dr. Cartwright, Sleep Disorder Service and Research Center, Rush-Presbyterian-St. Luke's Medical Center, 1653 West Congress Parkway, Chicago, IL 60612.

Supported by NIMH grant MH-40052.

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TABLE 1. Characteristics of Volunteers Undergoing Marital Separation and Subgroup Chosen for Sleep Study

Characteristic	Entire Group			Sleep Subjects		
	Men (N=110)	Women (N=104)	Total (N=214)	Men (N=35)	Women (N=35)	Total (N=70)
Age (years)						
Mean	36.3	34.7	35.2	37.7	35.0	36.4
SD	6.1	5.9	6.1	5.7	5.7	15.9
Number of children						
Mean	2.1	2.2	2.1	2.0	2.0	2.0
SD	1.1	1.3	1.1	0.8	1.1	1.0
Subjects with no children						
N	31	33	64	14	14	28
%	28	32	30	40	40	40
Education						
High school						
N	16	17	33	1	4	5
%	15	16	15	3	11	7
College						
N	74	66	140	27	22	49
%	67	64	65	77	63	70
Advanced						
N	20	21	41	7	9	16
%	18	20	19	20	26	23
Number of months separated						
Mean	8.8	6.7	7.3	8.4	7.1	7.8
SD	10.5	9.7	10.2	8.4	3.5	6.5
Spouse who left						
Husband						
N	59	45	105	17	16	33
%	54	43	49	49	46	47
Wife						
N	45	50	94	17	15	32
%	41	48	44	49	43	46
Both or neither						
N	6	9	15	1	4	5
%	6	9	7	3	11	7

tance to, an affective disorder and for investigating the presence and persistence of associated sleep disturbances over time. The data to be reported here address the following questions:

1. What is the frequency of early REM sleep in people who are in the process of divorce who meet diagnostic criteria for major depressive disorder?
2. What is the frequency of this sign in people who are in the process of divorce who do not meet diagnostic criteria for depression?
3. How often does early REM sleep persist following remission of depressive symptoms?
4. What is the predictive value of early REM sleep among depressed subjects for later adjustment to the process of divorce?
5. What is the role of a family history of depression or alcoholism in the presence and persistence of early REM sleep?

METHOD

The subjects for the sleep studies were drawn from a pool of 214 volunteers who met the following inclusion criteria.

1. They were all undergoing the breakup of a first marriage that had lasted at least 3 years. One partner

had left the home and/or filed for divorce. If the divorce had already been granted it had to have been within the previous 3 months.

2. The men had to be 25 to 50 years old. To avoid the possible confound of menopause, the women had to be 25 to 45 years old. None of the women was postpartum.

3. All had to be able to read and write English.

4. All had to agree to return 1 year later for a follow-up study.

The one exclusion criterion was that they all had to be free of any antidepressant or other REM-sleep-suppressing medication.

Table 1 describes the entire study group and shows that the smaller group chosen for the sleep study was a good representation of the total group on the demographic variables.

Subjects were recruited by advertising in neighborhood and city newspapers and were screened by telephone for the inclusion and exclusion criteria. Individual appointments were set up; during these interviews the study was explained, informed consent forms were signed, and a marital history interview was conducted by one of us (R.D.C.). Following this, each subject completed a self-administered battery of test instruments consisting of the Beck Depression Inventory (5), the Social Adjustment Scale (6), the Personal Adjustment

TABLE 2. Subjects Undergoing Marital Separation Who Met Diagnostic Criteria for Major Depressive Disorder at Baseline and 1-Year Follow-Up

Subjects	N	Met RDC		Had Beck Score of 14 or Higher		Met Both Criteria	
		N	%	N	%	N	%
Entire group at baseline	214	112	52	80	37	67	31
Men	110	51	46	37	34	28	25
Women	104	61	59	43	41	39	38
Entire group at follow-up	140	18	13	27	19	13	9
Men	67	10	15	11	16	6	9
Women	73	8	11	17	23	7	10
Sleep study group at follow-up	38	6	16	8	21	7	18
Men	19	4	21	4	21	4	21
Women	19	2	11	4	21	3	16

Questionnaire (7), the Who Are You (8), the Adjective Check List (9), and two versions of a social network instrument, one to list and rate the closeness of people in the respondents' network during the marriage and a second to describe their network since separating from their spouses. These instruments were chosen to sample the domains of self-reported mood disturbance, sex role identity, adjustment, personality, and social support. Data from only some of these instruments will be reported here.

Each volunteer then met with one of us (H.M.K. or C.I.E.), who conducted the Schedule for Affective Disorders and Schizophrenia (SADS) (10) interview and applied the Family History Research Diagnostic Criteria (FH-RDC) (11) in order to determine if a Research Diagnostic Criteria (RDC) (12) diagnosis of current major depressive disorder applied, whether there had been a previous episode of this disorder, and whether there was a family history of major affective illness. A Hamilton Rating Scale for Depression (13) score was also derived from this interview. All volunteers were paid a small fee.

The criteria for dividing the group into depressed and nondepressed subgroups were both a positive clinical diagnosis of major depressive disorder according to RDC and a Beck Depression Inventory score of 14 or higher. Unless otherwise noted, subjects labeled depressed or not depressed were classified according to both of these criteria.

Twenty depressed men, 20 depressed women, 15 nondepressed men, and 15 nondepressed women participated in a 3-night sleep laboratory study. The data analysis was based on these 70 subjects, 61 of whom returned to be rediagnosed and to complete their 1-year follow-up sleep studies. Thirty-eight (95%) of the 40 subjects who were depressed and 23 (77%) of the 30 subjects who were not depressed at baseline returned for the follow-up studies.

At follow-up, a single overall 10-point rating of post-divorce adjustment was made by one of us (R.D.C.) and

a blind rater on the basis of an interview that assessed each subject's current functioning in the areas of work, children, friends, home, finances, relationship with ex-spouse, mood, and sleep. The reliability of the scores made by these two raters was very high ($r=0.88$; the mean \pm SD for the first rater was 6.41 ± 2.04 and the mean for the second rater was 6.08 ± 1.93).

At both baseline and follow-up, the 3 nights of four-channel polysomnography were conducted on consecutive nights. On the first 2 nights the sleep was uninterrupted, and on night 3 dream collections were made from each REM sleep period. The REM latency was calculated by averaging the latency to REM sleep on nights 2 and 3, measured by using the Rechtschaffen and Kales (14) criteria and subtracting all wake time between sleep onset and the first REM period. A mean REM latency equal to or less than 60.5 minutes was defined as short.

RESULTS

Table 2 gives the number of subjects in the entire study group who were given the diagnosis of major depressive disorder according to RDC and Beck Depression Inventory scores at baseline and the number of subjects in the entire study group as well as in the sleep study group given the diagnosis at follow-up. This table shows that when seen close to the time of marital separation (baseline), approximately half of the subjects met RDC criteria, more than a third met the Beck criterion, and about 30% met the combined criteria for major depressive disorder. However, only a few continued to meet both criteria after 1 year. The sex ratios for depression (1:1.39 at baseline and 1:1.16 at follow-up for the entire study group) were much closer to equal in this study group than has been reported in the past but may reflect the tendency toward equalization between the sexes that has been noted recently (15). Among the 38 patients selected for the sleep study who met both criteria for depression and who returned for evaluation after 1 year, 18% still met both criteria at follow-up. More men than women were still depressed (table 2).

The first question we addressed was the frequency of early REM sleep in the 70 untreated volunteer subjects who were going through a stressful event (divorce). When tested initially, 21 (30%) of the 70 sleep subjects met the short REM latency criterion (onset of REM sleep in less than 60 minutes), and 49 (70%) did not. The second question we asked concerned the specificity of short REM latency to current depression. Fifteen (71%) of the 21 subjects with short REM latency and 25 (51%) of the 49 subjects without short REM latency also met both of our criteria for depression; six (29%) of the subjects with and 24 (49%) of those without short REM latency were not currently depressed. The significance of the association of short REM latency to a current depression was tested by a two-by-two chi-square analysis. A short REM latency was not significantly related to a current affective disorder in these

TABLE 3. Relation of Depression to REM Latency at Baseline and 1-Year Follow-Up of 61 Subjects Undergoing Marital Separation

Depression Status ^a	REM Latency at Baseline (min)		REM Latency at Follow-Up (min)		Correlation		
	Mean	SD	Mean	SD	r	df	p
Depressed at baseline and at follow-up (N=10) ^b	82.59	26.16	85.77	21.57	0.73	9	<0.01
Depressed at baseline but not at follow-up (N=28)	74.89	26.03	79.18	38.66	0.13	27	n.s.
Not depressed at either time (N=23)	90.30	35.21	79.94	33.77	0.62	22	<0.01
Total (N=61)	81.96	30.20	80.55	34.25	0.38	60	<0.01

^aDepression defined as positive clinical diagnosis of major depressive disorder according to RDC plus Beck Depression Inventory score of 14 or higher.

^bIncludes three subjects with an RDC diagnosis of probable depression at follow-up.

TABLE 4. Relation of REM Latency to Depression Status, Adjustment, and Family History of Depression at 1-Year Follow-Up of 38 Subjects Undergoing Marital Separation Who Were Depressed at Baseline

REM Latency	Depression Status According to RDC and Beck Score (≥ 14) ^a			Good Adjustment Rating ^b	Family History of Depression
	Met Two Criteria	Met One Criterion	Not Depressed		
Short at baseline and at follow-up (N=7)	0	0	7	5	5
Short at baseline and normal at follow-up (N=7)	2	3	2	2	2
Normal at baseline and at follow-up (N=21)	5	9	7	6	12
Normal at baseline and short at follow-up (N=3)	0	2	1	0	3
Total (N=38)	7	14	17	13	22

^aSignificant difference among diagnostic groups ($\chi^2=12.02$, $df=6$, $p<0.05$).

^bScore of 6–10 on the 10-point rating of post-divorce adjustment.

subjects ($\chi^2=1.5$, $df=1$, n.s.). However, four of the six subjects with short REM latency who were not depressed had recently recovered from an episode according to the SADS interview. When the currently depressed and recently depressed were combined and a two-by-two chi-square recomputed, the result was highly significant ($\chi^2=9.8$, $df=1$, $p<0.01$).

The REM latency marker was also not as sensitive for this group as has been reported for inpatients. Only 38% of the depressed subjects in this study showed this sign, in contrast to rates of 60%–70% reported for inpatient groups, but this is in line with the percentages of 30%–50% reported for outpatients (16). Since REM latency has been found to vary inversely with the severity of the depressive illness, perhaps some of the subjects in this group of nonpatients were too mildly depressed to show this sign. It is possible that their symptoms differed from those of the patient groups studied in the past (17–21).

The Beck Depression Inventory mean score of the 40 depressed subjects (22.23 ± 5.2) is in line with that reported for patient samples, but the mean Hamilton score of these subjects (12.00 ± 6.50) was lower. In previous studies, Reynolds and Kupfer (1) reported that REM latency and Hamilton scores correlated at about -0.70 . This correlation was not significant in the entire sleep study group of 70 subjects ($r=-0.08$, $df=69$) or in the depressed sleep study subgroup ($r=0.16$, $df=39$). Clearly, this group of nonpatients was judged by clinicians to have fewer of the somatic symptoms that are more heavily weighted in the Hamilton scale than in the self-report Beck measure (22), and this lower range of scores may account for the lower correlation.

The third question related to the stability of this marker over time. This was investigated by correlating the initial and follow-up mean REM latency for the 61 subjects who returned for the 1-year follow-up, divided into three subgroups: those who were depressed at baseline and remained depressed at follow-up, those who were depressed at baseline but who were no longer depressed at follow-up, and those who were not depressed at either time. The correlation for the group as a whole was modest but statistically significant (table 3). In general, REM latency tended to be stable over a year's time. However, the subjects whose status changed from depressed to not depressed had less stable REM latency over the period of a year than those who remained depressed or who were not depressed on either occasion.

Table 4 shows the depressed patients divided into those with short and normal REM latency at the two test points. More subjects who were depressed and had a normal REM latency continued to be depressed after 1 year (two-thirds still met one or both of the criteria). Only slightly more than one-third of the 14 subjects who were initially depressed and had short REM latency met one or both criteria at follow-up. All seven subjects who met neither depression criterion at follow-up continued to show REM latency at or below 60 minutes. Results of a four-by-three chi-square analysis of the initial and follow-up REM latency groups and the follow-up depression status on the two criteria were significant (table 4). This finding speaks to the fourth question, the predictive value of a short REM latency for later recovery. None of the subjects with a stable short REM latency remained depressed at the follow-up point.

This question of the predictive value of the shorter REM latency was also approached in terms of the subjects' ability to cope with the issues in their lives. The 10-point rating scale for adjustment to the divorce was dichotomized so that a scores of 1–5 indicated poor adjustment and scores of 6–10 indicated good adjustment. Twenty (87%) of the 23 subjects who were not initially depressed were rated as having made a good adjustment at follow-up, but only 13 (34%) of the 38 subjects who were initially depressed did as well (table 4).

The subjects who were depressed but who had a normal REM latency were slower to get over the divorce and to handle their life issues appropriately, but most of the subjects with a trait-like short REM sleep on both occasions had scores indicating good adjustment (table 4), in contrast to the findings for the subjects whose initially short REM latency normalized a year later. Only two of these seven patients had scores indicating good adjustment. Although the numbers are rather small for any definitive statements, it appears that, if depressed, having a stable, trait-like, short REM latency may predict a lifting of the depression and a better life adjustment 1 year after a stressful life event.

Finding that this sleep "abnormality" was associated with a higher rate of recovery and a better adjustment to the new life circumstances raises the question of what other variables are associated with this sign that may help account for this finding.

Data on family history reported in table 4 show that many of those who originally met both of our criteria for depression recalled a positive family history of depression. Many of the subjects with a stable short REM latency recalled such a history. These data are retrospective in nature, which is not the most reliable way to obtain a family history. In fact, the numbers must be interpreted cautiously given the relatively high rate of positive family history of depression and/or alcoholism (43%) reported by the 23 subjects who were not depressed. Nonetheless, it shows some tendency for subjects with short REM latency to have a stronger family history of depressive disorders. This does not help to explain the more positive outcome of this group.

Other possibilities that were explored were the effect of age. Since REM latency normally shortens as delta sleep becomes shorter with age, perhaps the subjects in this study who had shorter REM latency were older. Among the depressed subjects the mean age of those with short REM latency was 36.44 ± 5.45 , which is not significantly different from the mean age of the depressed subjects with normal latency (36.54 ± 5.50). In fact, there was no age difference between the depressed and nondepressed subjects in this study (35.56 ± 5.46 versus 36.42 ± 5.51). There was also no significant sex difference between the subjects with short and normal REM latency.

The last factor explored to account for the relation found between recovery and short REM sleep was the presence of any subsequent treatment. Among the 38 depressed subjects who returned for 1-year follow-up, only four reported receiving any pharmacological treatment for depression in the interval. All four were in the

normal REM latency group. Sixteen reported having some psychotherapy or marital counseling, ranging from 8 weeks to a year. Those reporting having any subsequent treatment had a somewhat lower mean score on the follow-up adjustment measure than those who did not (4.9 ± 1.8 versus 5.3 ± 1.7). Intervening therapy did not appear to account for the greater improvement in the short REM latency group. Only four of these subjects had received any treatment at all, and they had a lower mean adjustment rating at follow-up than those who had not (5.2 ± 0.8 versus 7.7 ± 1.2).

CONCLUSIONS

A large group of volunteer subjects who were undergoing marital separation and/or divorce had a surprisingly high rate of major depression according to rather conservative criteria. In line with other studies of outpatients, 38% showed a short latency to the first REM sleep. However, this sign was not specific to those with a current diagnosis of major depressive disorder but was present in those with a current or recent episode. Half of those who showed this sign while depressed on first testing continued to show this sign a year later, although none met the study's depression criteria at that point. These subjects had both higher rates of recovery from depression and better life adjustment than those depressed subjects who maintained normal REM latencies. These findings suggest that a short REM latency may show not only a persistent, perhaps genetic, vulnerability to an affective response to a major stressful life event but also a greater capacity to recover from it. The subjects with and without this sleep sign were equally depressed on a self-rating scale that emphasizes cognitive/affective symptoms, but the subjects with short REM latency had more severe scores on a scale that weighs core depressive features more heavily.

It is possible that this volunteer group represents a truncated piece of a severity continuum. However, in this kind of community study group the short REM latency sleep sign was associated with a shorter course of depression and better life adjustment without formal treatment.

The main finding of the paper warrants some rethinking of the meaning of a short REM latency as a sleep "abnormality" and further exploration of individuals who are clinically depressed but who do not have this marker. It would also be of interest to explore the personality characteristics and the dreams that accompany short versus normal REM latency in the presence of depressive symptoms. Perhaps these data may enlighten us about the psychological differences between these groups. It appears that it is depressed individuals who do not have the short REM latency sleep indicator who need more vigorous intervention. There are some data showing that those who do not have this sign are not likely to respond to the tricyclic antidepressants, which suppress early REM sleep (23). As Vogel et al. (24) have suggested, individuals who do not have short REM la-

tency may fail to build REM pressure when REM-deprived by medication, behavioral awakenings, or the early morning awakenings characteristic of their sleep (25). It is possible that we are dealing with two types of affective disorder: one more episodic and the other more chronic. The subjects with short REM latency need to be followed at shorter intervals and for longer periods of time to trace their relapse rate and to discover the predictive power of this marker as an indicator of future vulnerability.

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Depression in Recently Bereaved Prepubertal Children

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Objective: The purpose of this study was to ascertain depressive symptoms in recently bereaved prepubertal children and compare these symptoms with those of depressed prepubertal children. **Method:** The subjects were 38 children who had recently experienced the death of one but not both of their parents. They had to meet strict inclusion criteria so that the effects of bereavement per se, rather than other significant stressors, could be assessed. The comparison group consisted of 38 hospitalized, depressed children individually matched to each bereaved subject for age, sex, and socioeconomic status. All of the children underwent systematic and comprehensive evaluation. They and their parents were independently evaluated by trained interviewers using the parent and child versions of the Diagnostic Interview for Children and Adolescents. Family histories and basic demographic information were also obtained. **Results:** The recently bereaved children endorsed many depressive symptoms. Thirty-seven percent of them met the DSM-III-R criteria for a major depressive episode. The depressed children, however, had more depressive symptoms on average than the bereaved children. The factors associated with increased depressive symptoms in the bereaved children were 1) the mother as the surviving parent, 2) preexisting untreated psychiatric disorder in the child, 3) family history of depression, and 4) high socioeconomic status. **Conclusions:** A considerable number of the bereaved children developed the clinical symptoms of a major depressive episode immediately after the death of a parent. The relation of these symptoms to the subsequent course of grief and to major depressive disorder remains unknown and should be studied further.

(Am J Psychiatry 1991; 148:1536-1540)

Four percent (approximately 1.2 million) of children in the United States experience the death of a parent before the age of 15 (1). However, there has been little systematic research on children's reactions to parental death and the relation of bereavement occurring in childhood to subsequent psychopathology (2). In particular, information regarding symptoms of depression experienced by bereaved children is not available. Without such information, accurate differentiation between normal grief and depression in children may not be possible.

In adults, grief has been empirically differentiated from depression. Factors reported to differentiate the two include feelings of worthlessness, marked psychomotor re-

tardation, and functional impairment (DSM-III-R). When present, these factors may indicate that bereavement is complicated by a major depressive episode. Studies of adults (3, 4) have provided useful models for studying bereavement in children. However, differences in social, emotional, cognitive, and physical development preclude assuming that bereavement reactions in children are identical to those of adults. Consequently, bereavement should be studied directly in children.

Previous studies of bereavement in childhood have been limited in several ways. In many studies, the subjects were children who were already receiving psychiatric treatment at the time of the parent's death (5-9). However, grief in psychiatrically ill children cannot be assumed to be similar to grief in normal children. Studies have also been limited by the use of subjective ratings rather than standardized rating scales to assess psychopathology (5, 6).

Studies of normal prepubertal children's reactions to parental death have been even more limited. Elizur and Kaffman (10) examined grief reactions in children aged 2-10 years whose fathers had died. Information from semistructured interviews with the children's mothers and teachers indicated that the children had sleep dis-

Received Dec. 20, 1989; revision received April 8, 1991; accepted May 20, 1991. From the Department of Psychiatry and the Neuroscience Program, The Ohio State University. Address reprint requests to Dr. Ronald A. Weller, Department of Psychiatry, The Ohio State University, Rm. 61, Upham Hall, 473 West 12th Ave., Columbus, OH 43210.

Supported in part by grants from the National Research and Information Center and the Ohio Department of Mental Health and a Bremer grant and a seed grant from The Ohio State University.

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turbance, social withdrawal, and restlessness. However, the subjects in both this study and another study (11) with similar results were children living on a kibbutz in Israel whose fathers had died in a national war. Thus, the findings may have limited generalizability.

Van Eerdewegh et al. (12) also reported numerous depressive symptoms following the death of a parent in children aged 2–17 years. The depressive symptoms included dysphoria, withdrawal, sleep disturbance, and anhedonia. More psychopathology was found in the children of psychiatrically ill (usually depressed) mothers. However, this information was obtained solely from ancillary sources (i.e., data were not obtained directly from the children). Failure to interview the child may result in underreporting of subjective symptoms such as dysphoria and anxiety (13).

The purpose of this study was to ascertain depressive symptoms in recently bereaved prepubertal children, compare and contrast the depressive symptoms in these bereaved children with those found in depressed children, compare parent and child reports of depressive symptoms, and determine risk factors associated with the development of depressive symptoms in the bereaved children.

METHOD

The subjects were 38 prepubertal children who had experienced the recent death of one but not both of their parents. To eliminate stressors other than bereavement as factors that could affect symptoms, we specifically excluded children of families with financial difficulties, chronic illness and/or psychiatric illness, or recent divorce in the nuclear family. Only children from families who met the following criteria were included: 1) at least one parent had been employed for the majority of the time in the preceding 2 years, 2) there was no chronic incapacitating illness in either the children or the parents other than that associated with the deceased parent's death, 3) no member of the nuclear family had had psychiatric treatment in the previous 2 years, and 4) when children of divorced parents were included, the divorce had occurred at least 2 years earlier, and the children had weekly contact with both parents. In addition, the surviving parent had to be able to be interviewed and complete the questionnaires.

The children we studied met the following additional criteria: 1) an IQ of at least 70, 2) no chronic incapacitating medical or psychiatric illness, and 3) ability to be interviewed and complete self-report inventories with assistance. Finally, the subjects had to live within 50 miles of the study center.

Virtually all deaths in this area are reported in the obituaries published in local newspapers, so these were used to identify bereaved families in which there was a surviving spouse and at least one child. The funeral home director or clergyman was contacted to discuss the nature of the study and the appropriateness of contacting the family. If it was considered appropriate, the

family was contacted, and if the family was willing, family members were screened to determine whether they met the inclusion criteria.

Of 101 potential study families with children aged 5–12 years who were within a 50-mile radius of the study center, 23 could not be contacted because phone numbers and addresses were unavailable. An additional 30 families did not wish to participate. Of the remaining 48 families, 26 met the inclusion criteria and consented to participate. Although we would have preferred a greater rate of participation, the rate in this study was comparable to that obtained in a previous study of bereavement which used a nonreferred sample (14).

The 38 bereaved children were aged 5–12 years (mean±SD=8.9±2.4 years), and about half (53%, N=20) were female. The number of children interviewed per family ranged from one to three (mode=1). For 23 children (61%) the parent's death was anticipated (e.g., from cancer), and for 15 (39%) the death was unanticipated (e.g., from cardiopulmonary arrest, stroke, or accident). Children whose parents' deaths were the result of suicide and homicide were not included. The surviving parents' ages ranged from 25 to 47 years (mean±SD=36.0±5.2 years), and most of these parents (73%, N=19) were mothers. Socioeconomic status, as assessed by the Hollingshead-Redlich index (15), ranged from upper (class I) to lower (class V), with most subjects in the middle class (class III). This bereaved sample has been previously described (16).

A comparison group of 38 depressed children was recruited from the child psychiatry inpatient unit at a university teaching hospital during the same period in which the bereaved children were recruited. The depressed children were individually matched to each bereaved subject for age (mean±SD=9.1±1.9 years), sex, and socioeconomic status.

Children and parents were independently and simultaneously evaluated by clinically trained interviewers. For the bereaved group, interviews occurred 3–12 weeks after the death of the parent (mean±SD=7.9±2.5 weeks). The inpatient depressed children were interviewed upon admission to the hospital. Although all interviewers were similarly trained, different interviewers assessed the bereaved and depressed groups. Prior to each interview, the interviewers met with the parent and child or children and explained the procedure. The interviews began after the parent gave informed consent and each child's assent had been received.

Multiple structured interviews and rating scales were used to evaluate the bereaved group. Those used for this particular study included the parent and child forms of the Diagnostic Interview for Children and Adolescents (17). These are structured interviews to establish the presence or absence of psychiatric diagnoses for the child on the basis of *DSM-III* criteria. For the purposes of this study, all subjects were asked all depression questions from this diagnostic interview regardless of whether they answered yes to the four cardinal questions at the beginning of the section that assesses depressive symptoms. The parents of the bereaved chil-

TABLE 1. Depressive Symptoms in 38 Bereaved and 38 Depressed Prepubertal Children as Reported by the Children and by Their Parents^a

Item	Child Report				Parent Report				Parent and/or Child Report			
	Bereaved Children		Depressed Children		Bereaved Children		Depressed Children		Bereaved Children		Depressed Children	
	N	%	N	%	N	%	N	%	N	%	N	%
Dysphoria	20	53	31	82 ^b	14	37	29	76 ^b	23	61	36	95 ^c
Loss of interest	13	34	21	55	8	21	26	68 ^d	17	45	32	84 ^c
Appetite disturbance	8	21	22	58 ^b	2	5	14	37 ^d	9	24	26	68 ^c
Sleep disturbance	11	29	28	74 ^d	3	8	26	68 ^d	12	32	35	92 ^c
Psychomotor agitation or retardation	12	32	25	66 ^d	4	11	13	34 ^e	14	37	29	76 ^d
Fatigue	3	8	18	47 ^d	1	3	20	53 ^d	4	11	29	76 ^c
Guilt/worthlessness	8	21	29	76 ^d	6	16	21	55 ^d	14	37	32	84 ^c
Trouble thinking	2	5	18	47 ^d	3	8	16	42 ^d	5	13	25	66 ^c
Morbid/suicidal ideation	18	47	29	76 ^b	11	29	24	63 ^d	23	61	34	89 ^d
Diagnosis of major depressive episode (DSM-III-R criteria)	10	26	28	74 ^f	3	8	25	66 ^f	14	37	36	95 ^c

^aAll comparisons are between bereaved and depressed children by McNemar's test.

^b $p < 0.01$.

^c $p < 0.001$.

^d $p < 0.005$.

^e $p < 0.05$.

^f $p < 0.0001$.

dren also completed the Psychiatric Diagnostic Interview genogram, a structured interview for obtaining a family history of psychiatric disorders based on *DSM-III* criteria (18).

The depressed children and their parents were administered the appropriate versions of the Diagnostic Interview for Children and Adolescents, but the parents did not complete the genogram.

Depressive symptoms were determined from the Diagnostic Interview for Children and Adolescents. Although the interview was designed for assessment according to *DSM-III* criteria, we developed a program to rescore the interview according to the *DSM-III-R* criteria for a major depressive episode. Items were grouped into nine symptom areas based on the *DSM-III-R* criteria: dysphoria, loss of interest, appetite disturbance, sleep disturbance, psychomotor agitation or retardation, fatigue, excessive guilt and/or worthlessness, trouble thinking, and morbid or suicidal ideation.

The frequency of individual symptoms of depression was calculated for each subject group in three different ways: 1) from the child's report only, 2) from the parent's report only, and 3) from both reports (if the child and/or the parent reported a symptom, it was scored as present). The third method, combining the reports of the parent and child, closely approximates the decision-making process in clinical practice.

RESULTS

Frequency of Depressive Symptoms in Bereaved Children

Symptom endorsement was least frequent for the bereaved children when only the parent's report was used (table 1). When only the child's report was used, endorse-

ments were more frequent. Symptom endorsement was most frequent when the child and parent reports were combined. A diagnosis of major depressive episode was more than three times as common when data from the child, rather than the parent, were used (26% versus 8%; $\chi^2=0.83$, $df=1$, n.s.). When both reports were used, more than one-third (37%) of the children met the *DSM-III-R* criteria for a major depressive episode.

Dysphoria, loss of interest, appetite disturbance, sleep disturbance, psychomotor agitation or retardation, guilt/worthlessness, and morbid/suicidal ideation were each reported by or for at least one-quarter of the bereaved children. While 61% of the bereaved parents and children specifically reported suicidal ideation in the children (i.e., thinking they would be better off dead, wishing they were dead, and/or having thoughts about killing themselves), no suicide attempts were reported. In contrast, 42% ($N=16$) of the depressed sample had made at least one suicide attempt according to the child's or parent's report.

Comparison of Bereaved and Depressed Children

The mean \pm SD number of depressive symptoms overall was 7.3 ± 2.2 for the depressed children and 3.2 ± 2.7 for the bereaved children.

Child report. The occurrence of individual depressive symptoms was reported less frequently by the recently bereaved children than by the inpatient depressed children (table 1). These differences were significant for all symptoms except loss of interest. Stepwise discriminant analyses indicated that the symptoms of guilt/worthlessness and fatigue (both more frequent in the depressed group) best discriminated bereaved from depressed subjects. By using these two symptoms, 74% of the bereaved children and 82% of the depressed children could be correctly classified.

Parent report. The data obtained from the parents yielded similar results. The frequency of each depressive symptom was significantly less for the bereaved than for the depressed children. Stepwise discriminant analyses found that sleep disturbance and fatigue best differentiated the depressed from the bereaved children. When evaluated together, these symptoms correctly classified 89% of the bereaved children and 71% of the depressed children.

Both reports. Similarly, when data from both child and parent reports were used, the bereaved children had significantly fewer depressive symptoms than the depressed comparison subjects in every case (table 1). In the stepwise discriminant analyses, every depressive symptom was used to differentiate the two groups accurately. The combined reports of symptoms correctly classified 84% of both groups.

Child Report Versus Parent Report

The depressed children and their parents reported more depressive symptoms than did the bereaved children and their parents. However, within both the bereaved and depressed groups, the children reported more depressive symptoms than their parents did. To assess the degree of disagreement between parent and child reports, the mean number of symptoms for each subject was calculated on the basis of the child's report and the parent's report. These scores were compared for bereaved and depressed children by using Student's *t* test (two-tailed). The mean number of depressive symptoms reported by the children was greater than that reported by the parents; this difference was significant for the bereaved group but not for the depressed group. The bereaved children reported a mean \pm SD of 2.5 ± 2.5 symptoms, compared to 1.4 ± 1.9 symptoms reported by their parents ($t=2.71$, $df=36$, $p<0.01$). The depressed children reported 5.8 ± 3.1 symptoms, compared to 5.0 ± 3.1 symptoms reported by their parents ($t=1.25$, $df=36$, n.s.).

Factors Associated With Depressive Symptoms in the Bereaved Children

Potentially important clinical and demographic factors were examined in relation to depressive symptoms. Student's *t* test (two-tailed, with Satterthwaite's correction for unequal variance [19] when appropriate) was used to determine whether the total number of depressive symptoms (as reported by both parent and child) varied as a function of the sex of the living parent, the sex of the child, the age of the child (i.e., older [those aged 10–12, $N=18$] versus younger [those aged 5–9, $N=20$]), sibling position in the family (e.g., first- versus third-born), type of death (unanticipated versus anticipated), preexisting untreated psychiatric disorder in the child, family history of depression, and socioeconomic status. In addition, the impact of age on specific depressive symptoms was determined.

The age and sex of the child and type of parental

death were unrelated to the overall number of depressive symptoms experienced. However, when specific depressive symptoms were considered, more guilt symptoms were reported for older children than for younger children (0.4 ± 0.5 versus 0.1 ± 0.3 ; $t=2.11$, $df=27.6$, $p<0.04$). When the mother was the surviving parent ($N=19$), more depressive symptoms were reported for the children (3.9 ± 2.6 versus 1.0 ± 1.8 ; $t=3.11$, $df=36$, $p<0.004$). The children who had preexisting untreated psychiatric disorders ($N=12$) experienced more depressive symptoms (5.3 ± 1.8 versus 2.3 ± 2.4 ; $t=3.84$, $df=36$, $p<0.0005$). A family history of depression ($N=24$) was also associated with more depressive symptoms in the child (3.0 ± 2.7 versus 1.6 ± 1.6 ; $t=1.89$, $df=34$, $p<0.07$).

Pearson correlation coefficients were used to determine whether the total number of depressive symptoms (as reported by parent and child) would be associated with sibling position in the family or socioeconomic status. While sibling position did not affect the number of depressive symptoms noted, children in families from the higher socioeconomic classes experienced more depressive symptoms ($r=0.35$, $df=36$, $p<0.03$).

DISCUSSION

In this study, bereaved children experienced numerous depressive symptoms but had fewer symptoms than inpatient children with major depression. Differences between the depressed and bereaved children may have been exaggerated by the fact that the depressed group was hospitalized, whereas the bereaved group was not. Comparison of bereaved children with outpatient depressed children, who might be less severely depressed, might yield different results.

Several interesting distinctions between grief and depression are suggested by the pattern of symptom endorsement in the two groups studied. Although the analyses indicated that guilt/worthlessness was a symptom that significantly differentiated depression from bereavement, 21% of the bereaved children did report this symptom. Do bereaved children with excessive guilt/worthlessness experience a more severe or an atypical reaction to bereavement, or do they develop a more "true" depressive episode? Long-term follow-up will be necessary to answer this question.

DSM-III-R suggests that in bereavement, "thoughts of death are usually limited to the person's thinking that he or she would be better off dead or that he or she should have died with the deceased person." While 61% of the bereaved children and/or their parents reported that the children had suicidal ideation, none had actually attempted suicide. By contrast, 89% of the depressed children and/or their parents reported suicidal ideation in those children, and 42% admitted at least one suicide attempt. It might be hypothesized that in bereaved prepubertal children, suicidal ideation represents a longing to be with the deceased parent (reunion fantasy) rather than the devaluation of one's own life.

This explanation was given by several subjects who reported suicidal ideation. If true, this might account for the absence of suicide attempts and the less frequent reports of feelings of worthlessness by the bereaved children. However, further study is needed to clarify this issue.

In regard to evaluating depressive symptoms, it should be noted that grieving parents were not fully cognizant of their children's depressive symptoms. Such parent-child differences in reporting symptoms have been observed previously (13). In the current study parental underreporting of depressive symptoms was significantly greater in the bereaved families than in the families of the depressed children. This underscores the importance of interviewing bereaved children directly and not relying solely on parents' reports of their children's symptoms.

Additionally, surviving fathers reported significantly fewer symptoms in their children than did surviving mothers. This finding should be the subject of further investigation. For example, were fewer symptoms reported because the children who had a father as the surviving parent actually had fewer symptoms or because the surviving fathers in this study were less aware than the surviving mothers of the depressive symptoms in their children? Since more fathers than mothers with children in this study's age range die, the answer to this question could potentially influence the frequency of depression reported in bereaved children.

Several factors previously associated with the development of depression in nonbereaved individuals were also correlated with the development of depressive symptoms in the bereaved children. Such factors included preexisting untreated psychiatric disorder, family history of depression, and socioeconomic status. Unfortunately, the small sample size and the possibility of type II statistical error (i.e., not finding a statistically significant difference when one actually exists) preclude definite conclusions at this time. The role of such potential risk factors for the development of depression in bereavement should be studied further.

Over one-third (37%) of these bereaved children met the *DSM-III-R* criteria for a major depressive episode, if criterion B(2) is ignored. This criterion states that a depressive episode should not be diagnosed when the disturbance is the normal reaction to death of a loved one (uncomplicated bereavement). Although normal reactions of adults to a loved one's death have been previously assessed, similar studies have not yet been done with children. Is a full-blown depressive episode that follows bereavement in some children different symptomatically, biologically, or etiologically from depressions that follow other highly stressful events or that

appear unrelated to any current life stressors? Clearly, this question remains unanswered. Family history studies and studies of biological markers in this population should provide some answers to these questions.

In this study, however, a considerable number of bereaved children developed the clinical picture of a major depressive episode immediately following the death of a parent. The relation of these symptoms to the subsequent course of grief or major depression remains unknown and should be the subject of further investigation.

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A Prospective Follow-Up Study of So-Called Borderline Children

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***Objective:** The purpose of this study was to ascertain the current diagnoses in late adolescence or early adulthood of children who had previously been diagnosed as "borderline." **Method:** This was a prospective follow-up study of 19 of a group of 32 children (ages 6–10) who had been diagnosed as "borderline" during their treatment at the Massachusetts Mental Health Center approximately 10–20 years earlier. Life history information was collected, and axis I and axis II diagnoses were assigned by use of the Structured Clinical Interview for DSM-III-R and unstructured clinical interviews. **Results:** The most significant finding was that, contrary to expectations, there were no axis I diagnoses of affective disorders or schizophrenia. On the other hand, axis II diagnoses were prevalent, and the overall outcome for the subjects was poor. Family stability was the only significant predictor of the relatively good outcome of five of the subjects. **Conclusions:** The childhood borderline diagnosis appears to be an antecedent of an array of adult personality disorders, but it is not associated with the adult borderline personality disorder per se, nor with axis I diagnoses.*

(Am J Psychiatry 1991; 148:1541–1547)

Until the past decade, most of the literature on borderline disorders of childhood consisted of rich yet anecdotal case reports focusing on psychodynamics or psychotherapeutic techniques (1–4). Children were described as "borderline" when their disturbance appeared to fall between neurosis and psychosis in terms of severity and manifest symptoms and their personality organization seemed similar to that described for adults with borderline states (5). These children displayed a psychotic mode of behavior under conditions of stress but neurotic or even normal functioning during times of greater emotional security.

In the early 1980s, objective criteria for the borderline child diagnosis were proposed by clinicians working with such children (6–8). Bemporad et al. (6, 7) identified five criteria on the basis of a review of the literature and their clinical experience with a group of children who seemed to be borderline and who had eluded appropriate placement in existing diagnostic

categories. These authors delineated five characteristic areas of disturbance: 1) fluctuation of functioning between neurotic and psychotic-like states secondary to environmental reassurance or threat, 2) difficulty in managing anxiety, 3) excessive fluidity of thought and poor differentiation between fantasy and reality, 4) difficulty in establishing relationships with others, except for relationships aimed at need fulfillment and excessive reliance on others to maintain internal stability, and 5) deficiency of control, including difficulties in managing anger, delaying gratification, and repressing primary process material. In addition, they noted that social awkwardness, uneven development, a high frequency of nonspecific neurological symptoms, and histories of physical and sexual abuse were prevalent in their group of borderline children. Bemporad et al. stressed that no one symptom was pathognomonic of the borderline child diagnosis but that the entire constellation of the syndrome had to be considered. While individual children might have had marked difficulties in specific areas of functioning, all borderline children in their original group exhibited difficulties in each of the five identified areas of disturbance.

In 1983 Vela et al. (8) proposed a diagnostic schema based on descriptions of borderline children in seven seminal clinical papers. The diagnostic criteria independently derived by these investigators represented a significant overlap with the criteria previously identified by Bemporad et al. This provided converging evi-

Presented at the 143rd annual meeting of the American Psychiatric Association, New York, May 12–17, 1990. Received Oct. 12, 1990; revision received April 18, 1991; accepted May 31, 1991. From the Department of Psychiatry, Harvard Medical School, Boston. Address reprint requests to Dr. Lofgren, McLean Hospital, 115 Mill St., Belmont, MA 02178.

Supported in part by a Milton Fund award to Dr. Lofgren.

The authors thank John G. Gunderson, M.D., and Sten B. Lofgren, M.D., for their critical readings of earlier versions of this manuscript. Copyright © 1991 American Psychiatric Association.

dence that borderline children are an identifiable group of psychiatrically disturbed children. In 1985 Benvenga et al. (9) demonstrated that use of the criteria established by Bemporad et al. (6, 7) reliably discriminated borderline children from two other groups of psychiatrically disturbed children. It was also found that the criteria clustered together statistically and were predictive of each other.

The clinicians who were proposing objective criteria for the borderline child diagnosis continued to use the label "borderline," although they noted that, in contrast to the spectrum of adult borderline personality disorder, the functioning of these children more closely resembled that of adults with pseudoneurotic schizophrenia as described by Hoch and Polatin (10). The term "borderline" was retained mainly because it had been used repeatedly in the previous literature concerning these children.

Although it may be possible to identify borderline children reliably, there is no evidence that this diagnosis has any predictive value. The few existing follow-up studies (11–14) have been inconclusive because of difficulties with sample size or inconsistencies in defining criteria (1, 8). One of the best clinical reports was by Kestenbaum (11), who retrospectively identified seven borderline children by using the criteria of Vela et al. (8); she reported extremely varied outcome for this small group. After 14–30 years, each of the seven was found to have a different diagnosis, ranging from anxiety neurosis to paranoid schizophrenia. This study suggested that there is no specific predictive validity for the borderline child diagnosis.

Other, larger follow-up studies, such as those by Etemad and Szurek (12), Wergeland (13), and Aarkrog (14), were limited by lack of clarity or lack of uniformity in initial or follow-up diagnoses. However, varied outcomes were noted in these studies as well. The results of other investigations (15, 16) also suggested that the borderline child diagnosis most likely describes an extremely indistinct psychiatric group.

One of the main questions that persists in the literature on borderline children is whether the borderline child diagnosis has any predictive value when a carefully identified group of borderline children is studied over time. Our prospective study was designed as pilot work prior to planning more systematic, controlled studies of the development of personality disorders. The specific purpose of this study was to determine the current diagnoses and outcome in late adolescence and young adulthood of a group of previously studied borderline children.

METHOD

The 19 subjects in this study were those available for follow-up 10–20 years later out of a group of 32 who, as latency-age children (ages 6–10 years), had been identified as borderline according to the criteria of Bemporad et al. (7). The children had been identified by agreement among

the independent ratings of three senior child psychiatrists who were familiar with the criteria of the borderline child diagnosis and who had extensive clinical experience with such children. Appendix 1 gives the list of symptoms used to evaluate the children in the borderline group. Children were excluded from this group if agreement on the diagnosis was not reached among the three raters or if criteria for any other concurrent psychiatric diagnoses (excluding neuropsychological diagnoses) were met. The first 24 of these 32 borderline children were described in several published reports (6, 7, 17, 18). All of them were selected from a large sample of hospitalized, severely disturbed children who were treated at the Massachusetts Mental Health Center between 1971 and 1984. At the time of the current study (1986–1990), the subjects were in late adolescence or young adulthood (ages 16–30 years).

All subjects in this study were assessed with two diagnostic methods at the time of follow-up. The first was the Structured Clinical Interview for DSM-III-R (SCID) (19), used to assign axis I and axis II diagnoses. When it was determined that a subject fulfilled criteria for a personality disorder, the personality disorder that most accurately described the subject's functioning was assigned by blind independent review of the SCID material by two of us (D.P.L. and J.B.). The second diagnostic method involved the administration of unstructured clinical interviews by one of the same two authors in the presence of the other. Both clinicians independently assigned diagnoses to each subject. There was a discrepancy in the diagnoses in one case only, and in that case the discrepancy was resolved by discussion. All diagnoses finally assigned by these two authors were in agreement with all of the *DSM-III-R* diagnoses assigned by using the structured interview.

Subjects were also assessed with the Global Assessment of Functioning Scale (GAF Scale), axis V of *DSM-III-R*. Three of the investigators (D.P.L., K.L., and G.O.) independently assigned GAF Scale scores based on reviews of all of the information collected on each subject (intraclass correlation between raters, 0.91). The final assessment tool was a Life History Questionnaire (20) adapted for use with this population. Information for these two instruments was collected from the subjects themselves, members of their immediate families, and, in many cases, clinicians who were familiar with the subjects.

RESULTS

Because we had been able to locate only 19 (59%) of the original 32 subjects, we first determined whether there were any systematic differences between the subjects who were located and those who were not. We found no differences between the groups on a number of baseline measures, i.e., sex, neurological findings, clinical characteristics, family stability, and histories of abuse. On this basis the subjects appeared to be representative of the original group.

The first major finding, which was unexpected, was

TABLE 1. Characteristics of 19 Subjects Who Had Received the Borderline Diagnosis at Ages 6–10 Years

Subject	Sex	Age (years)	Stable Family	GAF Scale ^a Score	Personality Disorder Diagnosis	Substance Abuse	Most Recent Living Situation
1	M	21		45	Antisocial	Yes	Prison
2	M	25		28	Paranoid		Hospital
3	M	30		29	Antisocial		Rooming house
4	F	16	Yes	38	Borderline		Group home
5	F	21		47	Schizoid		Brief, unstable living situations
6	M	19		34	Antisocial	Yes	Brief, unstable living situations
7 ^b	M	19	Yes	58	Avoidant		Family
8 ^b	F	19	Yes	54	Avoidant		Family
9	M	20		33	Borderline	Yes	Residential school
10	F	21		46	Borderline	Yes	Halfway house
11	M	21		44	Schizotypal		Family (recently, residential school)
12 ^b	M	18	Yes	83	None		Family
13	M	18		53	Schizoid		Family
14 ^b	M	18	Yes	83	None		Family
15	M	25 ^c		33	Antisocial	Yes	Family and rooming house
16 ^b	F	17	Yes	79	None		Adoptive family
17	M	17		50	Narcissistic		Sporadic, unstable living situations
18	M	21		29	Antisocial	Possible	Shelter for the homeless
19	M	25		51	Schizoid		Family

^aGlobal Assessment of Functioning Scale, axis V of DSM-III-R.

^bGood-outcome subject.

^cDeceased at age 25.

that there were no DSM-III-R axis I diagnoses of affective disorders or schizophrenia in the entire group at follow-up. However, 16 the 19 subjects had axis II personality disorder diagnoses (table 1). Only three of the 16 subjects with personality disorders were judged to have a primary axis II diagnosis of borderline personality disorder. A more common diagnosis was antisocial personality (N=5).

Six of the 19 subjects were noted to be substance abusers. All six of these subjects had either borderline or antisocial personality diagnoses.

Detailed medical histories were obtained, and all subjects in the study were reported to be in excellent physical health.

The subjects were divided into two groups on the basis of their functioning at the time of follow-up. A subject was considered to have a good outcome if he or she was functioning adequately in school, in a job, or both; good social adjustment outside the work area was not a criterion for good outcome. Five of the 19 subjects met the criterion for good outcome, and the other 14 were considered to have poor outcome. The five subjects with good outcome were also found to have the highest five GAF Scale scores (mean=71, range=54–83). This indicates that their functioning was indeed higher than that of the other subjects (mean score=40, range=28–53) even when criteria other than work or school functioning were taken into account.

Chi-squares were computed for all of the main dichotomous variables in the study. To control for multiple tests, the alpha level was set at 0.01, reducing Tukey's familywise error rate for all chi-squares taken together to 0.05. Subjects with stable families were more likely to be the good-outcome subjects ($\chi^2=9.98$, $df=1$, $p=0.005$, $\phi=0.64$). Subjects with stable families

were less likely to have personality disorder diagnoses ($\chi^2=7.72$, $df=1$, $p=0.005$, $\phi=0.64$) and were marginally less likely to have attended residential schools ($\chi^2=4.55$, $df=1$, $p=0.03$, $\phi=0.49$). Subjects with personality disorder diagnoses ($\chi^2=9.98$, $df=1$, $p=0.002$, $\phi=0.72$) and subjects who had had residential school placements ($\chi^2=7.54$, $df=1$, $p=0.006$, $\phi=0.63$) tended to have a poor outcome.

A logistic regression was computed to evaluate the efficacy of the dichotomous variables of diagnosis, family stability, and residential school placement in predicting good and poor outcome. These three variables significantly predicted the outcome categories of the subjects ($F=29.28$, $df=3, 15$, $p=0.001$) and accounted for 85% of the variance on the outcome measures. Of these three variables, family stability was the best predictor of outcome.

A multiple regression was also computed with the continuous GAF Scale scores as the outcome measure. Because the variables were highly intercorrelated, a principal component score of 0–3 was also assigned to each subject, and a simple regression was then computed for the principal component and GAF Scale scores. A subject was assigned 1 point for having no personality disorder diagnosis, 1 for never having been placed in a residential school setting, and 1 for having a stable family. The component scores were highly correlated with both the GAF Scale scores ($r=0.90$, $df=18$, $p=0.001$) and the categorical outcome measures ($r=0.93$, $df=18$, $p=0.001$). The component factor accounted for 80% of the variance on the outcome measures.

Family stability was the most striking predictor of outcome in this study. Only six families in this group had been rated as stable by the original investigators.

TABLE 2. Current and Recent Employment Histories of 19 Subjects Who Had Received the Borderline Diagnosis at Ages 6–10 Years

Subject	Occupation/Training	Other Means of Livelihood
1	Unemployed, community college dropout	Drug dealing, car theft, shoplifting, pickpocketing
2	Occasional sheltered workshop, special schools, high school dropout	
3	Unemployed, high school graduate	Public assistance
4	High school student	Shoplifting, car theft
5	Community college student, part-time semiskilled labor (difficulty holding jobs)	Shoplifting, public assistance, support by others
6	Unemployed, high school equivalency diploma	Support by older woman, car theft, theft and assault, probable prostitution, public assistance
7 ^a	College student, camp counselor in summer	
8 ^a	High school student, part-time unskilled labor	
9	High school student (at age 20) in residential special school	
10	Full-time skilled labor, high school graduate (difficulty holding jobs)	Prostitution, drug dealing
11	High school student, special classes	Theft, shoplifting
12 ^a	Full-time unskilled labor, high school graduate	
13	Sporadic semiskilled jobs, high school graduate (difficulty holding jobs)	
14 ^a	High school student, part-time semiskilled labor	
15	Residential school, high school dropout	Car theft, assault
16 ^a	High school student, part-time unskilled labor, camp counselor, plans to attend college	
17	Unskilled jobs, currently unemployed, high school graduate (difficulty holding jobs)	Prostitution, stealing from family, public assistance
18	Unemployed, cannot hold unskilled jobs, expelled from residential school	Prostitution, borrowing money
19	Unemployed, college graduate (attended college 8 years)	

^aGood-outcome subject.

The five subjects with the best outcome came from five of these six families. One of the 14 subjects with poor outcome came from the sixth stable family. Family stability was negatively correlated with *DSM-III-R* axis II diagnoses. Of the five subjects with good outcome, three did not meet the criteria for personality disorders, although two of these three were noted to be shy and somewhat anxious. The remaining two subjects with good outcome met the criteria for avoidant personality. Only two of the good-outcome subjects had axis II diagnoses, while all 14 of the poor-outcome subjects did. These findings indicate that subjects who grew up in stable families were less likely to have personality disorders as young adults and were more likely to have a good outcome.

An evaluation of the GAF Scale scores and personality diagnoses together revealed an orderly picture. The top half of the group in terms of functioning tended to have either no personality disorder diagnosis or a schizoid or avoidant personality diagnosis (one subject had a narcissistic personality diagnosis). The subjects in the bottom half of the functioning ratings tended to have borderline or antisocial personality diagnoses (one subject had a schizotypal and one a paranoid personality diagnosis). Because of the group size, the only potentially meaningful mean±SD GAF Scale scores for the separate diagnoses were those for no personality diagnosis (81.7±1.7), schizoid personality (50.3±3.8), borderline personality (39.0±6.6), and antisocial personality (34.0±6.6).

The group's overall level of functioning was quite low. Even two of the subjects with good outcome were living quite limited lives. This overall low level of functioning is reflected in the GAF Scale scores. The overall mean±SD GAF Scale score was 48.0±18.2. The mean score is in the marginally adjusted range; the standard

deviation scores fall within the incapacitated to fair ranges in terms of functioning (21).

We found that no subject was self-supporting and living independently. Whereas two subjects, 16 and 17 years old, were at an age at which independence would not be expected, for the others the failure to become independent may have been more reflective of developmental failure. Nine of the 19 subjects were living with their families (table 1). Only five of these were attending school or work on a regular basis, and these were the subjects with the best outcome (table 2). Two subjects had found ways to be taken in and supported by people outside their families—one by the family of a boyfriend and one by a lover who was an older woman. One subject was a recluse supported by public assistance who lived alone and was awake only at night. One subject was currently in prison, one was staying occasionally in a shelter for the homeless (otherwise, he had lived on the streets since he burned down his family's home a few years earlier), one was in a state hospital, and one had died following an automobile accident. He had had multiple hospitalizations and multiple residential school placements and had been struggling with alcoholism at the time of his death. The remaining three subjects had never been able to survive outside of institutions and continued to live in residential group settings. At least four subjects had been involved in prostitution and the sale of illegal drugs or theft.

Although five subjects had satisfying relationships with their families (all five were good-outcome subjects), only three of them reported having satisfying friendships with peers. Nine subjects, including two of the subjects with good outcome, reported having no friends or social life at all, and seven subjects reported only highly tumultuous relationships. Only one subject, now a widow leading an extremely unsettled existence, had married.

Family stability showed a nearly significant negative correlation with residential school placement. Eleven of the 19 subjects had been placed in residential schools following the 1–4 years of treatment at Massachusetts Mental Health Center that all subjects had received (table 3). None of the good-outcome subjects had had residential school placements. It is likely that having had an unstable family situation increased the probability of residential school placement. However, the psychiatric (and other societal) interventions necessary for this group as a whole were long-term and expensive. Even the good-outcome subjects and/or their parents had received long-term outpatient treatment.

Of particular interest, given the strong predictive value of family stability, is the beneficial influence of restoration of a supportive family environment. Three of the five subjects with good outcome had originally been in destructive family situations. Two of these three families had improved substantially as a result of family therapy and individual therapy of the parents, and they had been considered stable by the original investigators by the time these children left treatment at Massachusetts Mental Health Center. The third child had been adopted into a stable family at age 8, during treatment. Thus, all three of these good-outcome subjects had had over 10 years of more healthy interactions with a family by the time of this follow-up study.

DISCUSSION

This study demonstrates a continuity of psychopathology from latency to early adult life. Children who met the borderline child criteria during latency, and who were neither neurotic nor psychotic, tended to continue to be neither neurotic nor psychotic but had personality disorders as adults. The criteria for the diagnosis of borderline children appear to provide a reliable means of identifying children who are at substantial risk for developing a range of personality disorders as adults. Thus, the childhood borderline syndrome might be conceptualized as a child version of Kernberg's borderline personality organization (22, 23), a midrange category that encompasses a variety of different personality disorders. Obviously, any relation between the childhood borderline diagnosis and borderline personality disorder as delineated in *DSM-III-R* has not been borne out. The borderline child diagnosis remains a misnomer. Instead, this diagnostic category appears to represent an antecedent condition for the development of an array of personality disorders in adulthood.

The absence of findings of axis I schizophrenic and affective diagnoses in this group is notable. Despite brief episodes of frankly psychotic behavior as children, none of the subjects exhibited schizophrenic symptoms as adults. And regardless of the presence of many affective features in the functioning of these subjects, both as children and as adults, none of them met criteria for major affective disorders. When borderline child symp-

TABLE 3. Psychiatric Treatment Since Index Treatment of 19 Subjects Who Had Received the Borderline Diagnosis at Ages 6–10 Years

Subject	Number of Hospitalizations	Other Psychiatric Treatment ^a
1		Long-term residential
2	≥ 3	Long-term hospital and residential
3		Short-term residential
4		Long-term residential
5		Long-term outpatient
6	≥ 3	Long-term sporadic outpatient
7 ^b		Long-term outpatient
8 ^b		Long-term outpatient
9	≥ 3	Long-term residential
10	≥ 3	Long-term residential
11		Long-term outpatient
12 ^b		Long-term school counseling in special school setting; long-term outpatient treatment for mother
13		Long-term residential
14 ^b		Long-term treatment for parents
15	≥ 3	Long-term residential
16 ^b		Long-term outpatient
17		Long-term residential
18	≥ 3	Short-term residential
19		Short-term residential and long-term sporadic outpatient

^aLong-term is defined as more than 3 years.

^bGood-outcome subject.

toms are present without concurrent schizophrenic or affective diagnoses, these appear to denote vulnerability to the development of axis II but not axis I disorders in adulthood.

The other major finding of this study is that despite the absence of axis I affective and schizophrenic diagnoses, the level of functioning of this group was quite low. As a result of the subjects' remarkably poor modes of adaptation, they were difficult to locate, since they seemed to have dropped out of normal social existence. Most of the adult subjects were at the severest extreme of the range of personality disorders and seemed capable only of a grossly restricted or aberrant form of everyday life from the standpoint of ego functions, object relations, or defense against affects. The modes of adaptation in adult life appeared to fall into either of two major categories: 1) escape into impulsive, antisocial action and substance abuse with little connection to or regard for others or 2) schizoid avoidance of societal demands or relationships through solitary pursuits. Both forms of adaptation precluded any ability to be self-supporting or to experience other aspects of usual adult autonomy and fulfillment.

Possible reasons for this poor outcome, in addition to the basic psychopathology present in childhood, might include the predominance of social and economic problems facing most of the families of the children in this study, which may have heavily burdened their attempts at recovery. In addition, only severely ill, hospitalized children were selected for study in the original group, as these met the proposed criteria for diagnosis with confidence. Children with milder illness may have better outcome. The borderline children in this study, by definition, failed at the tasks of

latency. Successful accomplishment of latency tasks, such as adaptation to and learning in structured school environments and formation of satisfying relationships outside the immediate family, may have long-term prognostic significance.

The most striking prognostic finding was that all subjects with good outcome came from stable families. It should be noted that three of the five good-outcome subjects had originally been in extremely chaotic family situations. Despite the small numbers, this finding suggests that interventions in the family situation may have a positive influence on outcome, even for children who have had very destructive familial influences up to and including early latency.

The present results do not resolve the question of whether the childhood borderline diagnosis refers to a valid, coherent, and exclusive group of children. However, the overall similarity of outcome—severe personality disorder without comorbid axis I schizophrenic or affective disorders—is suggestive of a kind of uniformity in this childhood condition. Borderline children appear to represent a nonpsychotic but chronic psychiatric group that demands an enormous amount of financial and other kinds of societal resources. Because of the ongoing costs associated with treating and failing to treat patients with this disorder, further studies in this area should be done. Future investigations should include larger, controlled prospective studies of so-called borderline children in order to ascertain whether different features of the childhood borderline condition are correlated with the eventual development of specific personality disorders and to identify other factors that may affect outcome in this group. Special attention should be paid to how to allocate clinical resources so that family functioning can be enhanced, since this was the main factor that was strongly related to favorable outcome in this study.

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Appendix 1. Symptoms Associated With the Major Areas of Psychopathology in Borderline Children

Fluctuation of Functioning

- Rapid decompensation secondary to minimal emotional stress, with rapid reintegration after reassurance from the environment
- Brief shifts from neurotic to psychotic ideation
- Recurrent intrusions of bizarre preoccupations and fantasies
- Extreme dependence of level of functioning on environmental support

Nature and Extent of Anxiety

- Inability to contain anxiety, with rapid escalation of anxiety to panic unless helped by figures in the environment
- Inability to utilize signal anxiety
- Basis of anxiety residing in fears of destruction, mutilation, and emotional annihilation
- Greater suffering from anxiety due to inadequacy of neurotic defenses and lack of psychotic reconstitutive symptoms

Thought Content and Processes

- Inadequate “synthetic ego functions,” with some gross distortions and concretizations but without stable delu-

- sions, hallucinations, or prolonged or profound loss of contact with reality
- 2. Excessive fluidity of thought between fantasy and reality, with inability to control potentially frightening avenues of association
- 3. Short "reality span," with recurrent but transient intrusion of grotesque and bizarre fantasy themes
- 4. Concern with survival manifested by poorly developed defenses (obsessions, phobias, extreme dependency, merging) to ward off possibility of catastrophic destruction
- 5. Proficiency in obscure areas of knowledge, with lack of awareness of practical, everyday matters
- 6. Heterogeneous cognitive defects

Relationships to Others

- 1. Immature attachments to need-fulfilling adults (merging, primitive identification, dependency)

- 2. Excessive reliance on others to maintain inner security; good functioning with trusted adults
- 3. Poor relationships with peers, inability to utilize intellectual talents in group situations

Lack of Control

- 1. Inability to delay gratification or tolerate frustration
- 2. Syncretic expression of anxiety and tension by action and aggression
- 3. Inability to contain inner life so that anxiety leads to action

Associated Symptoms

- 1. Social awkwardness, lack of adaptiveness
- 2. Neurological "soft" signs
- 3. General unevenness in development

Trauma Experiences, Posttraumatic Stress, Dissociation, and Depression in Cambodian Refugees

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***Objective:** The authors' goal was to determine the levels of trauma and psychiatric symptoms in a randomly selected group of Cambodian refugees and to determine the relationship between the amount of trauma experienced and subsequent psychiatric symptoms. **Method:** Data on traumatic experiences and symptoms of posttraumatic stress, dissociation, depression, and anxiety were collected on 50 randomly selected Cambodian refugees who had resettled in the United States. **Results:** Subjects experienced multiple and severe traumas and showed high levels of all symptoms measured. Forty-three (86%) of the subjects met DSM-III-R criteria for posttraumatic stress disorder, 48 (96%) had high dissociation scores, and 40 (80%) could be classified as suffering from clinical depression. Correlations between trauma scores and symptom scores and among symptom scores were moderate to large. **Conclusions:** These results indicate that a high proportion of Cambodian refugees who are not psychiatric patients suffer from severe psychiatric symptoms and that there is a relationship between the amount of trauma they experienced and the severity of these symptoms.*

(Am J Psychiatry 1991; 148:1548-1551)

The experience of psychological trauma has long been thought to cause particular psychological symptoms (1). Van der Kolk (2) described the human response to overwhelming and uncontrollable life events as "remarkably consistent" (p. 2). Symptoms of anxiety, depression, and dissociation have been observed in groups such as war veterans, victims of natural disasters, and assault victims, and a cluster of anxiety symptoms has been identified that makes up the syndrome of posttraumatic stress disorder (PTSD).

Cambodian refugees are among the groups who have experienced severe psychological trauma. They were survivors of a holocaust in which an estimated one to three million of a population of seven million Cambodians were killed (3). Cambodians who were not killed were removed from their homes and forced to work in labor camps. Most of those who were able to avoid or escape from the labor camps traveled on foot to Thailand to reach refugee camps. These treks were characterized by extreme fear, danger, and deprivation. Life in Thai refugee camps was arduous, and there was con-

stant fear of disease and starvation. Cambodian refugees experienced severe traumas such as the death of spouses, children, relatives, and friends; witnessing the death and torture of others; being subject to severe physical and sexual violence; being forced to leave their homes; and losing all their possessions (3-5). Several studies have found that Cambodian refugees have experienced even more trauma than other Southeast Asian refugee groups (5, 6).

Many studies have examined psychiatric symptoms in groups of Southeast Asian refugees who were psychiatric patients. Several researchers have reported high levels of depression in Southeast Asian refugee patients (3, 5-7). Very high rates of PTSD have also been reported in groups of refugees who were psychiatric patients (3, 6-8). For example, in a group of 52 psychiatric patients who were Southeast Asian refugees, 71% met *DSM-III* criteria for a diagnosis of major affective disorder and 50% met *DSM-III* criteria for PTSD (6).

Research is beginning to explore the relationship between traumatic experiences and psychiatric symptoms in refugee groups. In a recent study of several Southeast Asian refugee groups, Kroll et al. (7) found that widows and those who had had traumatic experiences had more psychiatric symptoms than others (7). Similarly, Mollica et al. (6) found that refugee patients with PTSD reported having twice as many traumatic experiences as those without PTSD.

Several authors (6, 8, 9) have commented on the importance of studying the prevalence of posttraumatic psychiatric symptoms in nonpatient groups of South-

Presented, in part, at the Sixth International Conference on Multiple Personality and Dissociative States, Chicago, 1989. Received Aug. 2, 1990; revision received March 19, 1991; accepted April 29, 1991. From the Department of Psychology, Beloit College, and the Department of Counselor Education, University of North Carolina at Greensboro. Address reprint requests to Dr. Carlson, Department of Psychology, Beloit College, 700 College St., Beloit, WI 53511.

The authors thank Sokhom Oum and Nan Khoun for translation of measures and interpreting during interviews.

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east Asian refugees. Studies have shown high rates of posttraumatic symptoms in nonpatient groups of refugees as well. In a study of Hmong refugees, Westermeyer et al. (10) found that 63% reported having mental or emotional problems since their arrival in the United States. This subgroup had significantly higher scores on every subscale of the SCL-90 than did Hmong refugees who did not report mental or emotional problems. In a study of 1,684 Southeast Asian refugees in California (5), more than 50% had high scores on two or more of four scales measuring anxiety, depression, difficulties in functioning due to emotional or nervous problems, and trouble with memory. Another large-scale study of several Southeast Asian refugee groups ($N=2,775$) (9) found that 10% met criteria for PTSD. Clearly, a substantial proportion of refugees who have not sought psychiatric treatment have considerable psychological difficulties.

The present study was undertaken to explore a number of questions not yet addressed in a single study. We were interested in the amount of trauma experienced by Cambodian refugees who are not psychiatric patients and the severity of their psychiatric symptoms, particularly symptoms of PTSD and dissociation. In addition, we sought evidence that dissociation and PTSD symptoms are universal (cross-cultural) responses to trauma. We were also interested in the relationship between the amount of trauma experienced and subsequent psychiatric symptoms. Finally, we wanted to examine the relationships among different types of symptoms in this traumatized group. We anticipated that the greater range of trauma and symptoms shown by a nonpatient group (compared with a patient group) would make statistical analyses more meaningful.

METHOD

Fifty adult subjects from a group of approximately 500 Cambodian refugees who had settled in Greensboro, N.C., between 1983 and 1985 participated in the study. Names of subjects were randomly selected from a list of all refugees resettled by a nonprofit social services agency. All came from rural areas and had no formal education. Twenty-six subjects were women and 24 subjects were men. Subjects ranged in age from 21 to 65 years with a mean \pm SD age of 42 ± 10 . Forty-nine subjects had never received any professional mental health care. All subjects participated voluntarily and gave fully informed consent.

Data collection was accomplished during interviews in subjects' homes by one of us (R.R.-H.) with the help of a native Cambodian translator, both of whom were known and trusted by all subjects because they had worked with the nonprofit social services agency to resettle the refugees when they first came to the area. Because most of the subjects were illiterate in their native language, all questions were read and reread to them in Cambodian.

Data on experiences of trauma were collected by us-

ing the Post-Traumatic Inventory (5). This 23-item questionnaire in Cambodian has a dichotomous (yes/no) answer format and was designed to inquire about the particular kinds of traumatic experiences reported by Southeast Asian refugees. (Examples of items are provided in the Results section.) Two questions were not asked of the subjects because the answers were the same for all: all were known to have lost all personal property and all had spent 1 year or more in a refugee camp.

A PTSD Checklist based on *DSM-III-R* diagnostic criteria for PTSD was created. For each symptom, subjects were asked to answer (yes or no) whether the symptom had happened to them recently. Five criteria were not included in the checklist because they were considered inappropriate to this group. Because of these omissions, the number of symptoms required to meet the criteria in the category of avoidance, detachment, and numbing was changed from three (out of seven) to two (out of three). Test-retest reliability of $r=0.85$ ($p<0.0001$) was established by administering the PTSD Checklist twice (with a 5-week interval) to 20 Cambodian refugees from a nearby city. This high degree of consistency indicates that the subjects understood the items.

The Dissociative Experiences Scale (11) is a 28-item measure of the frequency of dissociative experiences, including loss of awareness of one's surroundings, amnesia, depersonalization, and derealization. It has been shown to be a reliable instrument with test-retest reliability of $r=0.84$ ($p<0.0001$) and a mean split-half reliability (across diagnostic groups) of $r=0.88$ (11). Validity of the scale is supported by replication of results for different diagnostic groups by several authors (12-14).

Translation of the PTSD Checklist and the Dissociative Experiences Scale was accomplished by translation into Cambodian and blind back-translation into English by Cambodian natives who were well-educated former teachers and had worked in the United States as translators for more than 3 years.

Depression and anxiety were measured with the Cambodian version of the Hopkins Symptom Checklist-25 (HSCL-25) (15). This has proved a reliable and valid instrument for measuring depression and anxiety in Southeast Asian refugees; its test-retest reliability is $r=0.89$ (15).

RESULTS

Table 1 shows the scores on all of the instruments for all the subjects. No differences were found in scores by gender on any measure. The length of time between leaving home in Cambodia to arriving in the United States (length of hardship) ranged from 3 to 6 years; the mean was 4.6 years.

Eighteen of the 21 trauma items on the Post-Traumatic Inventory were endorsed by more than 50% of the subjects. The nine most frequently endorsed items (endorsed by at least 80% of the subjects) were 1) feel-

TABLE 1. Scores of 50 Cambodian Refugees on Measures of Trauma, Dissociation, Depression, and Anxiety^a

Variable	Mean	SD	Lowest Score	Highest Score
Total score on Post-Traumatic Inventory	14.1	3.6	8.0	21
PTSD Checklist score	11.7	2.8	4.0	14
Dissociative Experiences Scale score	37.1	16.1	9.3	88.6
HSCL-25 depression score	2.29	0.68	1.13	4.0

^aHigher scores indicate higher levels of trauma, dissociation, depression, and anxiety.

ing that one's life was in danger, 2) serious food shortage, 3) feeling that friends or relatives were in danger, 4) having a relative who disappeared, 5) having friends who disappeared, 6) change in residence because of proximity to battle area, 7) having friends forced to move in, 8) having relatives forced to move in, and 9) change in residence for economic reasons. Twenty-four (48%) of the subjects reported being physically assaulted (including rape), 31 (62%) reported having a friend killed while trying to leave Cambodia, and 29 (58%) reported having a family member killed while trying to leave Cambodia. As noted, all subjects had lived in a refugee camp for more than 1 year and had lost all of their personal property.

Forty-three (86%) of the subjects met the modified *DSM-III-R* criteria for PTSD. The mean number of PTSD symptoms endorsed by the seven subjects who did not meet the criteria was 8.4. Twenty (40%) of the subjects endorsed all 14 items on the PTSD Checklist.

According to the criteria of Mollica et al. (15) (an HSCL-25 depression score greater than 1.75), 40 (80%) of the subjects could be classified as suffering from clinical depression. Forty-three (86%) of the subjects met the criteria of Mollica et al. (15) for substantial emotional distress (HSCL-25 anxiety, depression, or total score greater than 1.75).

Table 2 shows Pearson correlation coefficients between symptom scores and their probability values. The only other significant correlation between variables was between Dissociative Experiences Scale score and age ($r=0.34$, $p<0.02$).

DISCUSSION

These results clearly show that these Cambodian refugees experienced multiple and severe traumas and had severe psychiatric symptoms at the time of the study. The levels of symptoms were strikingly high in view of the fact that this was a randomly selected group of refugees rather than a group of patients seeking mental health treatment. These results indicate that response to trauma is global, not specific, and that trauma victims are likely to meet criteria for more than one *DSM-III-R* diagnosis.

Our subjects' responses to the questions on the Post-

Traumatic Inventory closely paralleled those of the Cambodian refugees studied by Meinhardt et al. (5). Endorsement rates for items in the two studies differed by more than 20% in only eight of 23 items. This consistency supports the validity of subjects' reports of traumatic experiences.

The percentage of patients who met the modified *DSM-III-R* criteria for PTSD (86%) was considerably higher in this study than in the study of Gong-Guy (9) (16.3% of 590 Cambodian refugees). PTSD rates reported in Cambodian psychiatric patients have been inconsistent. Mollica et al. (6) reported that 57% of a group of Cambodian refugee psychiatric patients met *DSM-III* criteria for PTSD, but Kinzie et al. (16) recently reported that 92% of a similar group met *DSM-III-R* criteria at the time of their hospital admission.

Differences in results between the present study and previous studies may be the result of differences in the experiences of subjects in the groups studied. Although other studies have not reported the length of time between leaving home in Cambodia and arriving in the United States, it is likely that subjects in our study spent substantially more time in labor camps, trekking to Thailand, and in refugee camps. The subjects in our study arrived in the United States between 1983 and 1985, but most of those in previous studies seem to have arrived between 1979 and 1982 (6, 9). It is possible that our subjects' experience of a longer period of hardship is responsible for their greater symptoms.

Dissociative Experiences Scale scores for this study group were high. Only two subjects scored within or near the range usually seen for normal adults (0 to 10), and the mean Dissociative Experiences Scale score for this study group (37.1) was comparable to that of a group of war veterans with PTSD (11). This is not surprising in view of the similarity of experiences and symptoms between refugees and veterans (8). It also supports the view that dissociation is a universal response to traumatic experiences.

High levels of depression and anxiety in this study group are consistent with rates reported in previous studies of refugees (5, 7, 9, 10). Eighty-one percent of the Cambodian psychiatric patients in the study of Mollica et al. (6) met criteria for major affective disorder. Sixty-nine percent of Cambodian psychiatric patients described in the study of Kinzie et al. (3) had experienced a major depressive episode.

The high levels of PTSD, dissociation, anxiety, and depression in this nonpatient group are pertinent to the debate over how individual personality characteristics affect responses to stress and whether preexisting psychopathology predisposes an individual to develop PTSD (17). Clearly, in this group, the vast majority of individuals had symptoms of PTSD. This supports the conclusion of Wilson et al. (18) that some extreme stressors will produce symptoms in almost everyone. This finding makes clear the importance of routine inquiry about the occurrence and severity of traumatic experiences in patients, especially when there is evidence of PTSD or dissociative symptoms.

TABLE 2. Correlations Between Measures of Trauma, Dissociation, Depression, and Anxiety in 50 Cambodian Refugees

Variable	PTSD Checklist Score		Dissociative Experiences Scale Score		HSCL-25 Depression Score		HSCL-25 Anxiety Score	
	r	p	r	p	r	p	r	p
Total score on Post-Traumatic Inventory	0.39	0.005	0.38	0.007	0.48	0.0004	0.35	0.01
PTSD Checklist score			0.37	0.008	0.59	0.0001	0.51	0.0002
Dissociative Experiences Scale score					0.57	0.0001	0.54	0.0001
HSCL-25 depression score							0.86	0.0001

Correlations between trauma scores and psychiatric symptoms show that the extent of trauma is moderately and positively related to the severity of symptoms of depression, anxiety, PTSD, and dissociation. The correlations are surprisingly high in view of the fact that their sizes were limited by the restricted ranges of scores in the study group (these subjects scored relatively high on all measures). In a less homogeneous study group (one that showed a wider range of trauma and symptoms), we would expect higher correlations between trauma scores and symptom scores. In addition, several variables that we did not measure (differences in the details of traumatic experiences, in experiences of posttraumatic social support and economic success, and in psychological predisposition) would be expected to contribute to the variance in observed symptoms. This makes the similarities in symptoms all the more striking.

A moderate correlation between Dissociative Experiences Scale scores and PTSD Checklist scores indicates that the two instruments measure related but distinct constructs. This is important to note because there was a high rate of dissociative symptoms in this group, but such symptoms are seldom noted or studied in trauma survivors. The high correlation between anxiety and depression scores shows a surprisingly strong relationship between these symptoms in this group.

In conclusion, it seems that a large proportion of Cambodian refugees still suffer from severe psychiatric symptoms 4–6 years after arriving in the United States. In addition to the high levels of depression, anxiety, and PTSD symptoms observed in previous studies, these people are also experiencing very high levels of dissociation. Finding these levels of psychological disorder in a nonpatient group is extraordinary and may reflect the natural course of PTSD when left untreated. In addition, results of this study provide empirical support for a relationship between the amount of trauma experienced and the severity of psychiatric symptoms.

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Symptoms of Eating Disorders in Patients With Obsessive-Compulsive Disorder

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Objective: This study was designed to explore potential overlap of the symptoms of obsessive-compulsive disorder and eating disorders. **Method:** The authors administered a structured, self-rating scale, the Eating Disorder Inventory, to 59 outpatients at an obsessive-compulsive disorder clinic and to 60 sex-matched normal volunteers. The Eating Disorder Inventory has been previously validated as a reliable measure of the specific cognitive and behavioral dimensions of the psychopathology typical of patients with eating disorders. The scores of the patients with obsessive-compulsive disorder and of the healthy comparison subjects were compared with those of 32 female inpatients with anorexia nervosa (N=10) or bulimia nervosa (N=22) who had also been given the inventory. **Results:** The patients with obsessive-compulsive disorder scored significantly higher than the healthy comparison subjects on all eight subscales of the Eating Disorder Inventory: drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, and maturity fears. Relative to the healthy subjects, male patients with obsessive-compulsive disorder had more symptoms than female patients with obsessive-compulsive disorder. The scores of the female patients with obsessive-compulsive disorder were midway between those of the 32 female patients with eating disorders and those of the 35 female normal subjects. **Conclusions:** These results suggest that patients with obsessive-compulsive disorder display significantly more disturbed eating attitudes and behavior than healthy comparison subjects and that they share some of the psychopathological eating attitudes and behavior that are common to patients with eating disorders.

(Am J Psychiatry 1991; 148:1552-1557)

There has been much recent interest in the clinical and biological overlap of obsessive-compulsive disorder and the eating disorders. Clinically, the focal and extreme preoccupation with food and body image characteristic of patients with anorexia nervosa and bulimia nervosa resembles to some extent the repetitive and ritualistic behavior exhibited by patients with obsessive-compulsive disorder (1-4). In addition to shared clinical features, there are biological similarities, since serotonin dysregulation has been implicated in obsessive-compulsive disorder, anorexia nervosa, and bulimia nervosa (5, 6). These factors have led to speculation concerning a potential link between obsessive-compulsive disorder and eating disorders (2-4).

Several studies have investigated a potential association between obsessive-compulsive disorder and eating disorders, but most have been neither controlled nor systematic in using validated rating scales to measure symptom overlap (2-4, 7). Of the several controlled studies, the majority have investigated retrospectively, through chart review, the prevalence of obsessive-compulsive disorder symptoms in patients with eating disorders (1, 2). One exception (8), however, used the National Institute of Mental Health (NIMH) Diagnostic Interview Schedule and found that 33% of the active bulimic subjects and 32% of the inactive bulimic subjects had met the DSM-III criteria for obsessive-compulsive disorder at some time in their lives. To our knowledge, there has been only one study (7) that specifically measured the current eating attitudes and behavior of patients with obsessive-compulsive disorder; that study had a small sample size, and the investigators concluded that there was no significant association between obsessive-compulsive disorder and the eating disorders.

Presented at the 143rd annual meeting of the American Psychiatric Association, New York, May 12-17, 1990. Received Sept. 26, 1990; revision received April 25, 1991; accepted May 31, 1991. From the Laboratory of Clinical Science, NIMH. Address reprint requests to Dr. Pigott, Bldg. 10, Rm. 3D/41, NIMH, 9000 Rockville Pike, Bethesda, MD 20892.

TABLE 1. Data on Patients With Obsessive-Compulsive Disorder or Eating Disorders and on Healthy Comparison Subjects Who Were Given the Eating Disorder Inventory

Variable	Patients With Obsessive-Compulsive Disorder (N=59) ^a		Healthy Comparison Subjects (N=60) ^b		Patients With Anorexia Nervosa (N=10) ^c		Patients With Bulimia Nervosa (N=22) ^c	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)								
Total group	37.4	10.2	30.8	9.7				
Females	38.1	12.1	28.6	8.7	23.7	10.0	22.7	2.6
Males	36.6	7.3	33.8	10.5				
Maudsley Obsessive-Compulsive Inventory score								
Total group	16.6	5.5	4.2	3.4				
Females	15.9	5.7	4.2	3.3	8.8	4.8	10.4	7.2
Males	17.9	5.1	4.3	3.5				
Body mass index	24.0	4.4	24.3	5.0				

^aTwenty-seven male and 32 female patients.^bTwenty-five male and 35 female subjects.^cAll female patients.

With this in mind, we administered the Eating Disorder Inventory (9) to 59 patients meeting the *DSM-III-R* criteria for obsessive-compulsive disorder. This is a 64-item self-report measure that consists of eight subscales measuring drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, and maturity fears.

Since the Eating Disorder Inventory focuses on the specific cognitive and behavioral dimensions that appear to be important in the development and perpetuation of the symptoms of patients with eating disorders, we wanted to assess patients with obsessive-compulsive disorder for the presence of the same characteristics. In previous studies, it has been shown that in large samples of patients with eating disorders and age- and sex-matched control subjects, the inventory reliably differentiates subgroups of patients with eating disorders and also distinguishes those with serious psychopathology from "normal" dieters (9).

While the Eating Disorder Inventory has been administered to large groups of young women (mean±SD age=20.3±1.6 years, N=271) and the results then compared to those for women with anorexia nervosa (aged 22.5±5.4 years, N=155) and bulimia nervosa (aged 22.6±4.0 years, N=92) (9), it has not been validated in older subjects (more than 30 years of age). Since our group of obsessive-compulsive disorder patients was older than the eating disorder and control groups previously reported, we recruited a comparison group specifically for this study. We also administered the Eating Disorder Inventory to a newly studied group of female patients with anorexia nervosa and bulimia nervosa in order to compare the obsessive-compulsive disorder group to a group of patients with eating disorders. Further, we chose to include men in both the group with obsessive-compulsive disorder and the comparison group because preliminary analysis indicated that the eating attitudes and behaviors of males with obsessive-compulsive disorder were at least as disturbed as those of females (10).

Our objectives for this study were 1) to assess systematically the eating attitudes and behavior of patients with obsessive-compulsive disorder as measured by the Eating Disorder Inventory and compare their scores to those of sex-matched healthy comparison subjects and 2) to compare the scores of our sample of patients with obsessive-compulsive disorder with those generally reported for patients with anorexia and bulimia nervosa.

METHOD

Fifty-nine outpatients (27 male and 32 female) at the NIMH obsessive-compulsive disorder clinic who met the *DSM-III-R* criteria for obsessive-compulsive disorder completed the Eating Disorder Inventory. At the time the inventory was administered, 23 (39%) of the patients had been medication free for at least 1 month, 21 (36%) were on a stable regimen of clomipramine, and 14 (24%) were on a stable regimen of fluoxetine. A body mass index was calculated from each individual patient's height and weight (11). Data on these patients are summarized in table 1.

The predominant obsessive-compulsive disorder symptoms manifested by the patients included checking and/or fear of harm (36%, N=21), cleaning and/or contamination fears (34%, N=20), repeating and/or preoccupation with numbers (19%, N=11), and scrupulousness (14%, N=8). Five (19%) of the men and six (19%) of the women reported obsessions or compulsions that were directly related to their body shape or appearance.

Among the female patients with obsessive-compulsive disorder, 44% (N=14) met the *DSM-III-R* criteria for an additional axis I diagnosis. The most common comorbid diagnosis was depression (34%, N=11), and an additional 13% (N=4) met the *DSM-III-R* criteria for a past episode of depression. In addition, among these patients, one met the criteria for generalized anxiety disorder, social phobia, and panic

TABLE 2. Eating Disorder Inventory Subscale Scores of Patients With Obsessive-Compulsive Disorder and Healthy Comparison Subjects

Eating Disorder Inventory Subscale	Total Group of Patients With Obsessive-Compulsive Disorder (N=59)		Total Group of Healthy Comparison Subjects (N=60)		Male Subjects Only			
	Mean	SD	Mean	SD	Patients With Obsessive-Compulsive Disorder (N=27)		Healthy Comparison Subjects (N=25)	
					Mean	SD	Mean	SD
Drive for thinness	3.8 ^a	5.1	1.9	3.1	3.3 ^b	4.5	1.0	1.6
Bulimia	2.0 ^a	3.9	0.5	1.5	2.1 ^b	3.9	0.2	0.5
Body dissatisfaction	11.4 ^a	8.5	6.2	8.1	9.0 ^c	7.2	3.2	5.4
Ineffectiveness	8.4 ^a	6.6	0.9	1.7	9.0 ^d	7.7	0.9	1.2
Perfectionism	7.3 ^a	4.4	5.2	4.3	6.4	4.7	4.4	3.5
Interpersonal distrust	4.2 ^a	3.7	1.3	1.8	5.3 ^c	4.1	1.6	2.2
Interceptive awareness	4.6 ^a	4.7	0.7	1.5	4.4 ^d	5.0	0.2	0.6
Maturity fears	3.5 ^a	4.4	1.3	1.6	3.9 ^b	4.4	1.6	1.9

^aSignificantly different from healthy comparison subjects ($p < 0.005$).

^bSignificantly different from male healthy comparison subjects ($p < 0.05$).

^cSignificantly different from male healthy comparison subjects ($p < 0.01$).

^dSignificantly different from male healthy comparison subjects ($p < 0.001$).

disorder, one met the criteria for simple phobia, and one met the criteria for agoraphobia with panic disorder. Among the male patients with obsessive-compulsive disorder, 10 (37%) met the *DSM-III-R* criteria for depression, two (7%) met the criteria for social phobia and generalized anxiety disorder, one (4%) had social phobia, and one met the criteria for generalized anxiety disorder. Further, two men (7%) had histories of agoraphobia with panic disorder, and three (11%) had histories of depression.

Sixty comparison subjects (25 male and 35 female) were recruited from local advertisements to complete a standardized battery of psychological tests including the Eating Disorder Inventory. All of the comparison subjects had been medication free for at least 3 weeks before entering the study. None of them had current or past significant medical or psychiatric disorders, as determined by a structured interview. All potential comparison subjects also completed the SCL-90-R (12), the Maudsley Obsessive-Compulsive Inventory (13), and the Beck Depression Inventory and were administered the Hamilton Rating Scale for Depression to exclude those with significant obsessive-compulsive disorder or depressive symptoms. A body mass index was also calculated for each of the comparison subjects. Data on these subjects are summarized in table 1.

Thirty-two female patients meeting the *DSM-III-R* criteria for anorexia nervosa (N=10) or bulimia nervosa (N=22) were administered the Eating Disorder Inventory at the time of their admission to the eating disorder unit at NIMH. Both groups of eating disorder patients had been free of psychotropic medication for at least 1 month before their admission. At the time the inventory was administered, the patients with anorexia nervosa were at 60%–70% of their calculated average body weight (14), and the bulimic patients were all within calculated normal weight limits. Table 1 presents data on these eating disorder patients.

The scores on the Eating Disorder Inventory were first analyzed by using multivariate analysis of variance

(MANOVA) to determine whether there were group or sex differences or any interaction of these factors when all variables were examined simultaneously. The criterion statistic in all MANOVA procedures was Wilks's lambda. Subsequently, data from the obsessive-compulsive disorder and comparison groups were compared by using a two-way analysis of variance (ANOVA) testing the main effects of group and gender and any interaction of the main effects for each subscale of the Eating Disorder Inventory. The effect of medication (obsessive-compulsive disorder group only) was evaluated in the same manner. The effect of age was evaluated by using an analysis of covariance procedure in which age was entered as the covariate in determining group and gender effects for each subscale of the Eating Disorder Inventory. All of our eating disorder patients were female, so only the female obsessive-compulsive disorder patients and comparison subjects were included in the comparative data analyses involving those patients. Again, a MANOVA was conducted to determine whether group differences existed when all variables were considered simultaneously. Subsequent one-way ANOVAs on each variable were accompanied by *t* tests with the Bonferroni correction ($\alpha = 0.05$) comparing female obsessive-compulsive disorder patients, healthy comparison subjects, anorexic patients, and bulimic patients. All data we report are expressed as mean \pm SD.

RESULTS

To ascertain whether there were any significant effects when all variables were considered simultaneously, we conducted a MANOVA comparing group (obsessive-compulsive disorder patients and healthy comparison subjects), gender (male and female), and Group by Gender effects. This revealed a significant effect for both group and gender ($F = 12.34$, $df = 8, 108$, $p < 0.0001$, and $F = 3.67$, $df = 8, 108$, $p < 0.0008$, respec-

TABLE 3. Eating Disorder Inventory Subscale Scores of Female Patients With Obsessive-Compulsive Disorder or Eating Disorders and of Female Healthy Comparison Subjects

Eating Disorder Inventory Subscale	Female Patients With Obsessive-Compulsive Disorder (N=32)		Female Healthy Comparison Subjects (N=35)		Female Patients With Anorexia Nervosa (N=10)		Female Patients With Bulimia Nervosa (N=22)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Drive for thinness	4.2	5.5	2.5	3.8	16.8	2.8	14.6	5.6
Bulimia	2.0	3.9	0.7	1.9	3.3	5.5	13.7	5.2
Body dissatisfaction	13.0 ^a	9.0	8.3	9.1	21.9	4.6	16.7	8.2
Ineffectiveness	8.4 ^b	5.6	1.0	2.0	18.0	8.9	15.8	8.8
Perfectionism	8.0 ^a	3.9	5.7	4.7	12.5	2.9	10.0	4.6
Interpersonal distrust	3.1 ^b	3.1	1.0	1.3	5.6	4.8	8.0	6.3
Interceptive awareness	4.8 ^b	4.3	1.0	1.9	11.9	6.5	16.5	8.6
Maturity fears	3.2 ^c	4.4	1.0	1.3	9.2	8.1	6.6	6.3

^aSignificantly different from female healthy comparison subjects ($p < 0.05$).

^bSignificantly different from female healthy comparison subjects ($p < 0.001$).

^cSignificantly different from female healthy comparison subjects ($p < 0.01$).

tively) but no interaction ($F=0.39$, $df=8$, 108 , $p>0.10$). Subsequent two-way ANOVAs comparing group (obsessive-compulsive disorder patients and healthy comparison subjects) and gender for each subscale of the Eating Disorder Inventory revealed that the obsessive-compulsive disorder patients scored significantly higher than the comparison subjects on all eight of the subscales (table 2). Only two of the eight subscales showed a significant gender difference: body dissatisfaction ($F=9.73$, $df=1$, 116 , $p<0.002$), where the women were more dissatisfied than the men, and interpersonal distrust ($F=6.92$, $df=1$, 116 , $p<0.01$), where the men were more distrustful than the women. There were no significant interactions on any of the subscales.

To evaluate whether the differences in subscale scores between the patients with obsessive-compulsive disorder and the normal comparison group might be attributable to a difference between the two groups in body size, the mean body mass indexes for the two groups were calculated. These were not significantly different ($t=-0.27$, $df=103$, $p=0.79$). According to the guidelines for the body mass index, the two groups had similar frequencies of obese subjects (obsessive-compulsive disorder patients, 9%; comparison subjects, 8%) and overweight subjects (obsessive-compulsive disorder patients, 22%; comparison subjects, 18%) (10).

Historically, with regard to gender, substantially more females than males meet criteria for anorexia and bulimia nervosa. In addition, on the Eating Disorder Inventory, female patients and control subjects have been shown to score substantially higher than male control subjects on each subscale (9, 15–17). With this in mind, it is surprising that in our groups the scores on only two of the eight subscales exhibited a significant effect for gender. To investigate this finding further, we compared the obsessive-compulsive disorder patients and the normal comparison subjects separately by gender.

The male obsessive-compulsive disorder patients scored significantly higher (each $p<0.05$) than the male comparison subjects on seven of the eight Eating Disorder Inventory subscales (table 2). Perfectionism was the only sub-

scale on which the scores were not significantly different. As indicated in table 3, the female obsessive-compulsive disorder patients scored significantly higher than the female healthy comparison subjects on six of the eight Eating Disorder Inventory subscales: body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, and maturity fears.

In the comparison of the female obsessive-compulsive disorder patients with the healthy female subjects, the anorexia nervosa patients, and the bulimia nervosa patients, the MANOVA revealed a significant effect for diagnosis when all variables were considered simultaneously ($F=12.67$, $df=24$, 255.8 , $p<0.01$). One-way ANOVAs with diagnosis as the main factor and post hoc comparisons revealed that the patients with anorexia nervosa and bulimia nervosa scored similarly on all of the Eating Disorder Inventory subscales except bulimia (table 3), on which the bulimic patients scored significantly higher ($F=26.3$, $df=1$, 31 , $p<0.001$). The bulimic and anorexic patients scored significantly higher than the healthy comparison subjects and the obsessive-compulsive disorder group on drive for thinness, interoceptive awareness, and ineffectiveness (each $p<0.05$). The bulimic patients scored significantly higher than the other groups on bulimia and interpersonal distrust (each $p<0.05$), and the anorexic patients scored significantly higher than the other groups on body dissatisfaction, perfectionism, and maturity fears (each $p<0.05$).

DISCUSSION

Our data demonstrate that patients with obsessive-compulsive disorder, in comparison to healthy subjects, display significant differences in the areas of eating and weight-related concerns as shown by scores on the subscales of the self-report Eating Disorder Inventory. The patients with obsessive-compulsive disorder scored significantly higher than the sex-matched healthy subjects on all of the subscales. Particularly intriguing is our find-

ing that male obsessive-compulsive disorder patients, in comparison to healthy male subjects, exhibited substantial pathology on the inventory. This finding is in striking contrast to the well-documented finding of higher scores on the Eating Disorder Inventory, as well as a greater incidence and prevalence of eating disorders, for women than for men (9, 15–17).

However, it is important to reiterate that the Eating Disorder Inventory was developed not as a diagnostic tool but to identify psychological and behavioral traits common in anorexia nervosa and bulimia nervosa. Accordingly, our finding that patients with obsessive-compulsive disorder have significantly elevated scores on the Eating Disorder Inventory in comparison to those of a healthy group cannot be used to conclude that obsessive-compulsive disorder patients have eating disorders but, rather, that they may share some of the same self-reported dimensions of psychopathology as patients with eating disorders.

With this in mind, we reviewed the eight subscales of the Eating Disorder Inventory for their intended item content. The subscales for ineffectiveness, perfectionism, interpersonal distrust, and maturity fears describe features common to many psychiatric populations; these include feelings of general inadequacy, excessive personal expectations, alienation concerns, and excessive dependency fears. Both the group with obsessive-compulsive disorder and the groups with eating disorders, not surprisingly, also endorsed these characteristics.

The remainder of the subscales reflect characteristics more specific to eating disorders. The patients with obsessive-compulsive disorder also scored significantly higher than the healthy comparison subjects in all of these areas. The subscales for bulimia and drive for thinness assess intense preoccupation with food as well as uncontrollable eating behavior. The subscales for body dissatisfaction and interoceptive awareness include items to detect body image distortion and inability to identify accurately emotions or visceral sensations of hunger or satiety. The higher scores of the obsessive-compulsive disorder patients on these subscales are particularly interesting, since they provide evidence that these patients endorse substantial dysmorphophobic and hypochondriacal concerns. They also provide evidence to support the hypothesis that patients with disorders characterized by extreme preoccupation with somatic symptoms or body image—such as monosymptomatic hypochondriasis, dysmorphophobia, hypochondriasis, and somatization disorder—may share many features with obsessive-compulsive disorder patients.

Several authors have suggested that there is significant comorbidity of obsessive-compulsive disorder and the eating disorders (1, 2, 7, 8). It is possible that our finding of significantly higher scores on the Eating Disorder Inventory for obsessive-compulsive disorder patients than for healthy comparison subjects is merely a reflection of a pervasive obsessional nature that involves all of their attitudes and behavior, including appetite and appearance. Alternatively, this finding may be evidence that patients with eating disorders and pa-

tients with obsessive-compulsive disorder share a common proclivity toward abnormal eating behavior and body image distortion.

While our group with obsessive-compulsive disorder was significantly older than the healthy comparison group, a separate analysis with age as a covariate failed to show evidence that age contributed significantly to the differences in the Eating Disorder Inventory scores. In addition, the scores of the comparison and eating disorder groups were similar to scores previously reported for larger, younger groups of anorexic patients, bulimic patients, and control subjects. Further, although the patients with obsessive-compulsive disorder were taking various medications, a separate analysis with medication as a covariate failed to show evidence that medication effects contributed significantly to the differences in the scores.

In summary, these results suggest that patients with obsessive-compulsive disorder display significantly more disturbed eating attitudes and behavior than healthy subjects and that they share some psychopathological traits and behavior with patients who have eating disorders. Perhaps most interesting is the finding that, in contrast to the healthy and eating disorder groups, men and women with obsessive-compulsive disorder exhibit similar disturbances in body image and eating attitudes and behavior as measured by the Eating Disorder Inventory.

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Extrapyramidal Symptoms Due to Dopamine-Blocking Agents in Patients With AIDS Encephalopathy

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Objective: The authors attempted to determine whether patients with AIDS are more susceptible to neuroleptic side effects than other patients. **Method:** Retrospective chart review was used to assess the frequency and severity of extrapyramidal symptoms in patients with AIDS and psychotic patients without AIDS who had taken dopamine-blocking agents. The charts of 804 men younger than 50 years were reviewed, and patients were excluded if they had not taken dopamine blockers, had taken them for more than 1 month, had received concomitant antiparkinsonian agents, had focal brain lesions or histories of Parkinson's disease or meningitis, had used cocaine, amphetamines, or opiates within 1 month of admission, or, among the comparison group, had HIV risk factors. For the remaining 31 AIDS and 32 comparison patients, age, duration of dopamine blocker treatment, dose in chlorpromazine equivalents, and nature and severity of parkinsonian complications were recorded. **Results:** The mean drug dose and body weight were significantly lower in the AIDS group. The likelihood of developing extrapyramidal symptoms was 2.4 times as high among the AIDS patients as among the comparison group. Such symptoms were developed by 50% of the AIDS patients who received less than 4 mg/kg of chlorpromazine equivalents per day and 78% of those who received more than 4 mg/kg per day. **Conclusions:** These preliminary results suggest that AIDS patients are more susceptible to extrapyramidal symptoms than psychotic patients without AIDS and that neuroleptics should be used cautiously and in lower doses for patients with AIDS.

(Am J Psychiatry 1991; 148:1558-1561)

Neuroleptic agents are often used to treat the psychiatric complications of AIDS encephalopathy. Both early and late in the course of the disease, agitation, delirium, and frank psychosis occur in about 10%-20% of AIDS patients (1). Recent pathological reports show loss of substantia nigra neurons in patients with AIDS encephalopathy (J. Artigas et al., unpublished study, 1989). AIDS patients, therefore, may have a higher risk of developing parkinsonism. Our clinical experience and several case reports (2-7) have shown greater susceptibility of AIDS patients to neuroleptic side effects, but, to our knowledge, no controlled studies have been done to substantiate these findings. In this study, we compared the frequency and

severity of extrapyramidal symptoms in AIDS patients and a comparison group of psychotic patients without AIDS.

METHOD

Subjects

The prevalence of extrapyramidal symptoms in patients taking dopamine blockers was assessed with a retrospective chart review. Included in the study were male patients under the age of 50 years who were treated with dopamine-blocking agents. These agents included neuroleptics and antiemetics. Patients with the following characteristics were excluded: 1) neuroleptic exposure for more than 1 month in the past, 2) simultaneous treatment with drugs having anticholinergic or dopaminergic properties, which have been shown to decrease the frequency of extrapyramidal symptoms when used prophylactically, 3) evidence of focal brain lesions on CT scan or history of meningitis or idiopathic Parkinson's disease, 4) use of cocaine, amphetamines,

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The authors thank Drs. Mark Nathanson, Pamela Call, and Ralph O'Connell for their help.

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or opiates immediately before admission, which could cause adventitious movements or rigidity, 5) unrecorded weight, and, in the comparison group, 6) risk for HIV infection (i.e., homosexuality, intravenous drug use, or blood transfusion). Cases were ascertained by reviewing all charts at an urban hospital of 1) male patients under the age of 50 years who had received the diagnosis of AIDS between January 1986 and June 1989 and 2) male patients of the same age diagnosed as having psychosis over the same time period.

Of the 804 charts reviewed, 741 were rejected: 205 patients (140 non-AIDS and 65 AIDS) had not been treated with neuroleptics or antiemetics, 423 (412 non-AIDS and 11 AIDS) had been given neuroleptics for more than 1 month, 18 non-AIDS patients had received neuroleptics and anticholinergic agents simultaneously, 35 (15 non-AIDS and 20 AIDS) had brain lesions, meningitis, or Parkinson's disease, 13 (11 non-AIDS and two AIDS) had used cocaine, amphetamines, or opiates before admission, six (three of each group) had no weight records, and 41 non-AIDS patients had HIV risk factors (31 used intravenous drugs and 10 were homosexual).

Procedure

Each patient's age, length of neuroleptic use, highest dose in chlorpromazine equivalents (8), and type of parkinsonian complications (with dates of occurrence) were recorded. Hoehn and Yahr staging (9) was used by the reviewers (E.H., T.K.) to semiquantify the severity of parkinsonian symptoms. This is a simple extrapyramidal symptom rating scale based on the level of clinical disability, which could be assessed relatively easily from the information available in the charts. The period reviewed for both groups was 1 month after the start of neuroleptic therapy.

The two-tailed Student's *t* test was used to analyze statistical differences between the means of the AIDS and non-AIDS groups with respect to continuous variables, i.e., neuroleptic dose, weight, and age. Where applicable, values are expressed as means plus or minus standard deviations. The Mantel-Haenszel odds ratio was used to estimate the relative odds of developing extrapyramidal symptoms in general and specific subtypes among AIDS patients versus the comparison group, adjusting for neuroleptic dose. The Mantel-Haenszel chi-square test was used to assess statistical significance. Exact 95% confidence limits for the assumed common odds ratio are also reported.

RESULTS

Thirty-one AIDS and 32 non-AIDS patients met the criteria and were included in the study. The mean chlorpromazine-equivalent dose was 301.1 ± 354.0 mg/day for the AIDS patients and 679.4 ± 610.4 mg/day for the non-AIDS patients; this difference was significantly different ($t=3.00$, $df=61$, $p<0.004$). Adjusted for body

TABLE 1. Relationship of Dopamine Blocker Type to Extrapyramidal Symptoms in AIDS Patients and Psychotic Patients Without AIDS

Dopamine-Blocking Agent	AIDS Patients (N=31)		Non-AIDS Patients (N=32)	
	Total	With Extrapyramidal Symptoms	Total	With Extrapyramidal Symptoms
Haloperidol	20	14	12	6
Molindone	0	0	1	0
Loxapine	0	0	7	3
Thioridazine	0	0	2	0
Chlorpromazine	0	0	7	5
Fluphenazine	1	1	2	2
Trifluoperazine	1	0	0	0
Metoclopramide	4	3	0	0
Prochlorperazine	4	0	0	0
Perphenazine	1	0	1	1

weight, the respective doses were 4.6 ± 5.2 and 9.1 ± 9.7 mg/kg per day, which were also significantly different ($t=2.30$, $df=61$, $p<0.03$). The weights of the AIDS and non-AIDS patients also differed significantly: 64.0 ± 7.8 and 77.6 ± 13.0 kg, respectively ($t=4.84$, $df=61$, $p<0.0001$). The mean age of the AIDS patients was 37.6 ± 7.6 years, and that of the non-AIDS patients was 34.9 ± 8.2 years (n.s.). Fifteen AIDS patients were homosexual, and nine used intravenous drugs; information on risk factors for HIV was unavailable for the rest. Of the 32 psychotic comparison patients, 21 were given diagnoses of schizophreniform disorder and 11 were diagnosed as having affective psychoses. The type of dopamine-blocking agents taken by the AIDS and non-AIDS groups are shown in table 1. Twenty-three patients in each group received high-potency dopamine-blocking agents.

Since the AIDS patients received a lower mean dose of medication than the comparison group, we divided each group into two subgroups: patients receiving less than 4 mg/kg per day and those receiving more than 4 mg/kg per day (table 2). Of those who received less than 4 mg/kg per day, 11 of the 22 AIDS patients and two of the seven non-AIDS patients had extrapyramidal symptoms. The odds ratio for developing extrapyramidal symptoms, comparing AIDS patients to non-AIDS patients, was 2.5 in the lower-dose group. In the group receiving more than 4 mg/kg per day, seven of the nine AIDS patients and 15 of the 25 non-AIDS patients had extrapyramidal symptoms. The odds ratio in this group was 2.3. The common Mantel-Haenszel odds ratio for the total group was 2.4.

The prevalences of the extrapyramidal symptom subtypes in the AIDS and non-AIDS groups were also compared. The AIDS patients were 2.4 times as likely to experience akathisia, 1.7 times as likely to experience dystonia, and 1.5 times as likely to experience rigidity (table 2). No patients in either group developed choreiform movements. Since chlorpromazine equivalents are only a rough estimate of a neuroleptic's ability to cause extrapyramidal symptoms, we also compared the fre-

TABLE 2. Odds Ratios for Development of Extrapyramidal Symptoms in AIDS Patients and Psychotic Patients Without AIDS Classified by Dopamine Blocker Dose

Extrapyramidal Symptom and Drug Dose (mg/kg/day)	AIDS Patients			Non-AIDS Patients			Common Odds Ratio	95% Confidence Interval	χ^2 (df=1)
	Total	With Symptom N	%	Total	With Symptom N	%			
All patients									
Any symptom	31	18	58.1	32	17	53.1	2.4	0.60–11.40	1.84
Dose < 4	22	11	50.0	7	2	28.6	—	—	—
Dose > 4	9	7	77.8	25	15	60.0	—	—	—
Dystonia	31	5	16.1	32	7	21.9	1.7	0.28–9.13	0.40
Dose < 4	22	2	9.1	7	0	0.0	—	—	—
Dose > 4	9	3	33.3	25	7	28.0	—	—	—
Akathisia	31	8	25.8	32	6	18.8	2.4	0.50–13.10	1.58
Dose < 4	22	4	18.2	7	1	14.3	—	—	—
Dose > 4	9	4	44.4	25	5	20.0	—	—	—
Rigidity	31	10	32.3	32	9	28.1	1.5	0.37–6.33	0.40
Dose < 4	22	7	31.8	7	1	14.3	—	—	—
Dose > 4	9	3	33.3	25	8	32.0	—	—	—
Patients taking haloperidol	20	14	70.0	12	6	50.0	3.4	0.40–38.60	1.64
Dose < 4	14	9	64.3	2	1	50.0	—	—	—
Dose > 4	6	5	83.3	10	5	50.0	—	—	—

quencies of extrapyramidal symptoms for patients treated with haloperidol, the most commonly used neuroleptic among both groups. The AIDS patients treated with haloperidol were 3.4 times as likely to develop extrapyramidal symptoms as the non-AIDS patients (table 2). All patients in the comparison group remained ambulatory (Hoehn and Yahr stages I–IV), and one AIDS patient became bedridden (Hoehn and Yahr stage V) but regained ambulation 2 weeks after withdrawal of the neuroleptic agent. Five patients in each group developed more than one type of extrapyramidal symptom.

DISCUSSION

In this study, the AIDS patients were estimated to be 2.4 times as likely to develop extrapyramidal symptoms as psychotic patients without AIDS. In the subset of patients treated with haloperidol, the estimated risk of developing extrapyramidal symptoms was 3.4 times as high among AIDS patients. We also found that AIDS patients were at higher risk of developing each of the various subtypes of extrapyramidal symptoms found among these patients (dystonia, akathisia, rigidity). The lack of choreiform or other dyskinetic movements in either group is probably due to the recent onset of neuroleptic use and short period of follow-up.

Although we estimated a higher risk of extrapyramidal symptoms in AIDS patients, we did not detect a statistically significant difference in the frequency of extrapyramidal symptoms overall or among the various subtypes of extrapyramidal symptoms. This lack of significance is likely the result of an insufficient number of patients in each group. Although we reviewed 804 charts, we were forced to exclude many patients in order to maintain comparability between the patient groups. Since we were interested in new cases of ex-

trapyramidal symptoms, we eliminated many potential subjects who had been treated with neuroleptics for longer than 1 month. Similarly, we eliminated patients treated with neuroleptics who either used recreational drugs before admission or had brain lesions, which could have confounded our results.

The mean dose of neuroleptics was significantly lower in the AIDS patients than in the non-AIDS group, even after adjustment for the lower weights of the AIDS patients. This dosing pattern was probably related to the physicians' suspicion that the AIDS patients would be more sensitive to neuroleptics.

Our comparison group was heterogeneous. Approximately two-thirds had schizophreniform disorder, and the remainder had affective psychoses. A study in which the non-AIDS patients all had affective types of psychosis might show a different relative risk in the AIDS and non-AIDS groups. It has been reported (10) that patients with affective psychoses have a higher rate of extrapyramidal symptoms than schizophrenic patients.

This study is limited by its retrospective nature. There were differences in the neuroleptic types and doses used for the two groups, and hospital charts were relied on for information about the nature and severity of extrapyramidal symptoms. A prospective study of extrapyramidal symptoms in patients taking similar doses of the same neuroleptic would be helpful. However, given the differences in prescribing patterns between AIDS and non-AIDS patients, such a cohort might be difficult to obtain. Comparison of AIDS patients receiving low- and high-potency neuroleptics would also be helpful. The physicians at our institution tended not to use low-potency neuroleptics to treat psychosis in the AIDS patients, probably to avoid anticholinergic toxicity. The data may also have been skewed by the possibility that AIDS patients received closer attention be-

cause of their medical condition. Nevertheless, the results support the hypothesis that AIDS patients are more susceptible to extrapyramidal side effects of dopamine-blocking agents than are non-AIDS patients.

Although a larger, controlled, prospective study would help confirm these findings, these data suggest that neuroleptics should be used cautiously and in lower doses in the treatment of AIDS patients.

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Emergency Psychiatric Assessment of Violence

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Objective: The purpose of the study was to 1) ascertain whether there are clinical and demographic characteristics that distinguish dangerous from nondangerous patients evaluated in a psychiatric emergency service and 2) identify variables that distinguish dangerous patients who are hospitalized from those who are not. **Method:** The authors conducted a case comparison study of 99 psychiatric emergency patients whom staff identified as dangerous to others, that is, violent or potentially violent. Clinical staff were interviewed and records reviewed. These data were contrasted with record review data for 95 nondangerous patients. **Results:** Log linear analysis showed that 1) variables relating to violence in community samples—age, sex, and past history of violence—related minimally or not at all to violence in this sample and 2) disposition to hospital versus community was associated with psychotic mental status and restraint in the psychiatric emergency service. Patients requiring restraint were more likely to have recently committed assault or battery and to have been brought in by the police. **Conclusions:** Enduring personal characteristics of patients relate neither to psychiatric emergency service assessments of current dangerousness nor to the decision to hospitalize. These determinations appear to be related to assessments of current patient state and immediate past behavior.

(Am J Psychiatry 1991; 148:1562–1565)

Under current civil commitment laws, psychiatrists make decisions to hospitalize mentally ill persons based in part on assessments of dangerousness to self or others. In many jurisdictions, imminence of violence is a requirement for commitment as a danger to others. A continuing problem for psychiatry is to identify those clinical and demographic variables that may be associated with patient violence and with the decision to hospitalize patients whom psychiatrists judge to be dangerous.

To date, studies of patient violence have yielded few clinically useful predictive relationships. Demographic variables associated with violence in general populations, e.g., youth, male sex, and unemployment, have not consistently related to violence in a clinical setting (1–5). No diagnosis has consistently related to patient violence, but clinical state variables—hostility, agitation, impulsivity, hallucinations, mania—have variably been reported to relate to inpatient violence (6–8). Studies of the emergency room decision for civil commitment have found a modest association between assessed dangerousness and severity of mental illness (9) and between impulsivity and commitment because of danger to others (10).

Our study had two objectives: to explore further 1) whether risk factors for violence in the community are also risk factors for violence in a psychiatric emergency room and 2) whether any situational, demographic, or clinical variable predicts hospitalization for dangerous patients.

METHOD

The setting was the psychiatric emergency service of a city hospital with a strong university affiliation. Psychiatrists, residents, nurses, and mental health workers staff the psychiatric emergency service.

The clinical staff identified all patients during a 6-month period who were evaluated as dangerous, that is, violent or potentially violent. The criteria for violence were evidence of assault or battery. The criteria for potential violence were verbal threat or staff concern about impending violence. Battery was defined as nonconsensual touching, assault was defined as a physical threat, and threat was defined as a verbal threat only. Staff concern was defined as current staff impression of poor control and anger or agitation. Staff identified 99 of 1,806 consecutive patients as study subjects.

Each patient was evaluated and treated as usual. Then, clinical staff completed a questionnaire covering demographic and clinical data; the type and context of the patient's violent behavior; and the assessment, treatment, and disposition of the patient.

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Dr. Frank Bernieri provided consultation on the statistical analysis. Copyright © 1991 American Psychiatric Association.

TABLE 1. Characteristics of Violent Psychiatric Emergency Patients (N=99) and Comparison Patients (N=95)

Characteristic	Violent Patients		Comparison Patients	
	N	% ^a	N	% ^a
Sex				
Male ^b	60	61	47	49
Female	39	39	49	51
Race				
White	70	80	—	—
Black	13	15	—	—
Asian	5	5	—	—
Work				
Full-time	8	8	—	—
Part-time	10	11	19 ^c	21
None	77	81	71	79
Marital status				
Single	56	63	54	60
Separated, divorced, widowed	20	22	16	18
Married	13	15	20	22
Living arrangement				
Alone	37	41	—	—
With family of origin	43	47	—	—
With spouse	11	12	—	—
Who accompanied patient to emergency room ^d				
No one	16	16	43	47
Police	36	37	14	15
Family	13	13	4	4
Mental health professional	24	24	31	34
Other	9	9	0	—
Restrained in emergency room ^e				
Yes	58	59	4	4
No	40	41	91	96
Disposition ^f				
Home	29	29	64	68
Hospital	61	62	27	29
Police custody	9	9	3	3
Type of violence in index episode				
Battery	36	36	—	—
Assault	20	20	—	—
Verbal threat	24	24	—	—
Other	19	19	—	—
Target of index violence				
Mental health worker	37	39	—	—
Family members	24	25	—	—
Police	18	19	—	—
Strangers/others	17	18	—	—
Current criminal charges				
Yes	17	32	—	—
No	36	68	—	—
Criminal record				
Yes	26	48	—	—
No	28	52	—	—
Type of past violence				
Battery	48	48	—	—
Assault	52	52	—	—
Threats	56	56	—	—
Number of previous psychiatric hospitalizations				
None	19	24	—	—
One to three	19	24	—	—
Four or more	42	52	—	—

TABLE 1 (continued)

Characteristic	Violent Patients		Comparison Patients	
	N	% ^a	N	% ^a
DSM-III-R axis I diagnosis				
Schizophrenia	20	20	—	—
Mania	18	18	—	—
Major depression	16	16	—	—
Alcohol abuse	14	14	—	—
Substance abuse	11	11	—	—
Other	20	20	—	—

^aSome data were missing; percents were based on number of subjects for whom data were available.

^b $\chi^2=2.67$, $df=1$, $0.10 > p > 0.05$.

^cIncludes all control patients employed part-time and full-time.

^d $\chi^2=36.92$, $df=4$, $p < 0.0001$.

^e $\chi^2=66.85$, $df=1$, $p < 0.0001$.

^f $\chi^2=29.17$, $df=1$, $p < 0.0001$.

Demographic and clinical data were obtained for a random sample of records of 95 nondangerous psychiatric emergency patients evaluated during the same time period; the study patients' records were excluded.

Statistics employed were chi-square analysis, log linear analysis, analysis of variance, and t test.

RESULTS

Table 1 presents data on the study and comparison patients. Of the study patients, 61% were men and 39% were women. Most were white, single, living alone or with family of origin, and unemployed, and most had been previously hospitalized. The mean \pm SD age was 33.7 \pm 11.1 years (median=31 years); 95% (N=96) were between 21 and 59 years old. The mean age of the comparison subjects was 37.2 \pm 13.0 years. The most common diagnoses of the study patients were affective disorder, schizophrenia, and substance abuse. Other diagnoses included panic, adjustment reaction, other psychosis, and bipolar disorder in remission. Current drug or alcohol use was present in 45% of the study patients.

Fifty-six of the study patients were violent; 43 were potentially violent. Sixty-three reported a history of violence. Sex and violence were related. Women more often were violent, and men more often were potentially violent ($\chi^2=8.93$, $df=3$, $p < 0.03$). Race, marital status, diagnosis, and intoxication did not relate to current or past violence.

Table 1 shows that there was a near significant tendency for study patients to be men, in contrast to the comparison patients. Study patients were 4 years younger ($t=2.02$, $df=193$, $p < 0.05$, one-tailed), were more often brought in by the police, less often came in alone, and were far more often put into restraints (59% versus 4%) or hospitalized (62% versus 29%).

Fifty patients (51%) were judged to be psychotic in the emergency room, that is, to be delusional or hallucinating or to have a severe thought disorder; 49 (49%) were not.

TABLE 2. Mental Status and Use of Restraint for Violent Psychiatric Emergency Patients (N=99) Who Were or Were Not Hospitalized^a

Mental Status and Restraint	Hospitalized ^b		Not Hospitalized ^b	
	N	%	N	%
Psychotic	39	85	7	15
Restrained	28	93	2	7
Not restrained	11	69	5	31
Not psychotic	21	49	22	51
Restrained	15	68	7	32
Not restrained	6	29	15	71

^aRelationship of disposition to mental status and use of restraint assessed with log linear analysis; the results of component chi-square analyses were as follows: mental status \times disposition— $\chi^2=13.53$, $df=1$, $p<0.001$; restraint \times disposition— $\chi^2=13.38$, $df=1$, $p<0.001$; mental status \times restraint \times disposition— $\chi^2=0.02$, $df=1$, n.s.

^bData missing for some patients.

Fifty-eight patients (59%) were placed in four-point restraints. Twenty-two patients (22%) were given intramuscular medication; 68 (69%) were not.

Sixty-one study patients were hospitalized, 29 returned to the community, and nine were retained in police custody. Four hospitalizations were voluntary; 57 were involuntary. The nine patients in police custody were excluded from further analysis, since the number was small and our interest was in disposition to hospital versus community.

Table 2 shows the relationship among psychosis, restraint, and disposition to hospital versus community and the results of the log linear analysis of these data. The analysis shows that psychosis and restraint were each independently related to disposition: psychotic patients and patients in restraints were more likely to be hospitalized.

In considering the relationship between restraint and disposition separately for psychotic and nonpsychotic patients, odds ratios show that psychotic patients who were restrained were 6.36 times more likely to be hospitalized than were psychotic patients who were not restrained ($\chi^2=3.17$, $df=1$, $0.10>p<0.05$). Nonpsychotic patients who were restrained were 5.36 times more likely to be hospitalized than nonpsychotic patients who were not restrained ($\chi^2=5.25$, $df=1$, $p<0.03$).

Table 3 shows that route to the emergency room and type of index violence related independently and significantly to restraint of dangerous patients. Patients brought in by the police more often were put into restraints than were patients who were brought in by others, who in turn were put into restraints more often than patients who came in alone. Table 3 also shows that patients who committed assault or battery were put into restraints more often than patients who made threats or were a source of concern to staff.

DISCUSSION

One limitation of our data is that we relied on self-report for history of violence. Thus, the failure of past violence to relate to demographics or to present violence may reflect unreliable reporting. However, we did review past

TABLE 3. Route to Emergency Room and Type of Violence in Restrained and Unrestrained Patients (N=99)^a

Variable	Restrained ^b		No Restrained ^b	
	N	%	N	%
Route to emergency room				
Brought by police	29	81	7	19
Brought by others	22	49	23	57
Came alone	6	38	10	62
Type of violence in index episode				
Assault or battery	40	73	15	27
Threat or other reason for concern	17	40	26	60

^aRelationship of disposition to mental status and use of restraint assessed with log linear analysis; the results of component chi-square analyses were as follows: route to emergency room \times restraint— $\chi^2=11.21$, $df=2$, $p<0.005$; violent episode \times restraint— $\chi^2=9.06$, $df=1$, $p<0.005$; route to emergency room \times violent episode \times restraint— $\chi^2=0.88$, $df=1$, n.s.

^bData missing for some patients.

clinical records as well as police records, and many of the patients were well-known to us. A further limitation is that for the comparison patients, information on past violence or criminal record was sketchy.

We found that dangerous patients were an average of 4 years younger than comparison patients and were much more likely to be men. Diagnosis, employment, and marital status did not distinguish dangerous patients from others. We conclude that these demographic variables and diagnosis do not distinguish dangerous patients from others with sufficient precision to be clinically useful.

These results are consistent with prior research showing that state variables but not more enduring characteristics are associated with restraint of emergency psychiatric patients (4, 5). The failure to find meaningful relationships between violence and demographics could be a result of methodological limitations, but we doubt it. We think these results reflect clinical reality. State variables are associated with patient dangerousness and disposition in a psychiatric setting; demographics are not. We found that patients who were brought to the emergency room by the police and patients who were more seriously violent frequently required physical restraint in the emergency room. Patients who required physical restraint or were psychotic were far more likely than other patients to need hospitalization.

These findings suggest that clinically important data are the patient's presentation in the psychiatric emergency service and reports of the patient's behavior in the immediate or recent past. The patient's enduring characteristics and diagnosis are of little help to the clinician in assessing current dangerousness and need for hospitalization.

Clearly, the same patient can present vastly different risks on different visits. The clinician must know how the patient was referred and the type of violent act and must assess the degree of self-control and whether or not psychosis is present.

Within the dangerous group, women were more violent than men. Women more often committed assault

or battery; men more often made threats or were a source of concern to staff. McNeil et al. reported similar findings on an inpatient unit (5). Perhaps these findings reflect the fact that women who make threats inspire less fear than men who do so. Women come to the attention of the psychiatric emergency service after they act; their talk causes less concern.

In conclusion, the decision of the psychiatric emergency service to hospitalize a patient may be the last in an ongoing acute episode that requires control: violence occurs, the police apprehend a psychotic subject, the emergency room restrains the subject, and the psychiatrist hospitalizes the subject. In other cases, the violence that leads to hospitalization occurs in the psychiatric emergency service. We did not adequately distinguish violence in the psychiatric emergency service from violence that began earlier. Future research should distinguish and examine situational variables in violence in the community versus the psychiatric emergency service.

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A Placebo-Controlled, Double-Blind Crossover Study of Fluoxetine in Trichotillomania

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***Objective:** It has been proposed by some investigators that trichotillomania, a disorder of chronic hair pulling, is a variant of obsessive-compulsive disorder, and some studies have suggested that the antiobsessional agents clomipramine and fluoxetine are useful in treating this disorder. The authors investigated the efficacy of fluoxetine in the treatment of trichotillomania. **Method:** Twenty-one adult chronic hair pullers were recruited into an 18-week placebo-controlled, double-blind crossover study of fluoxetine, in doses up to 80 mg/day. The fluoxetine and placebo treatment phases consisted of 6-week trials of each agent separated by a 5-week washout period. Fifteen subjects (14 female and one male) completed the study; an additional female subject dropped out at 16 weeks after developing a drug reaction. **Results:** No significant Drug by Period interactions were found in weekly subject ratings of hair pulling, weekly subject ratings of the urge to pull hair, weekly assessments of the number of hair-pulling episodes, or the estimated amount of hair pulled per week. **Conclusions:** The short-term efficacy of fluoxetine in the treatment of trichotillomania was not demonstrated in this study.*

(Am J Psychiatry 1991; 148:1566-1571)

Trichotillomania is a disorder of recurrent hair pulling that is included in *DSM-III-R* under "impulse control disorders not elsewhere classified." The condition has traditionally been considered to be rare, although some authors speculate that it may be more common than previously believed (1). Hair pulling may involve any hair site, but the scalp, eyelashes, and eyebrows are most frequently affected (1, 2). Although trichotillomania can occur in isolation, comorbidity with affective disorders, anxiety disorders, substance abuse/dependence, and eating disorders appears to be common in outpatient populations (2). Hair pulling has also been noted in psychotic patients (3-5) and in institutionalized mentally retarded populations (6).

Reported treatments for trichotillomania have included behavior modification (reviewed by Friman et al. [7]), hypnosis (8, 9), and psychodynamically oriented psychotherapy (10). Case reports of successful pharmacotherapy have included treatment with

isocarboxazid (11), amitriptyline (12), imipramine (13, 14), and chlorpromazine (5). In a recent study, eight of 10 patients with trichotillomania responded to lithium (15).

Observed similarities between trichotillomania and obsessive-compulsive disorder (16) have led to trials of antiobsessional (17) serotonin reuptake blockers in trichotillomania. Primeau and Fontaine (18) reported the successful use of fluoxetine in a case of trichotillomania. Recent reports of open trials of fluoxetine involving 3-18 trichotillomaniac patients (19-21) suggest that fluoxetine is effective in reducing hair-pulling behavior. In the only controlled study of medication treatment of trichotillomania, Swedo et al. (16) compared clomipramine to desipramine in 13 patients in a 10-week double-blind crossover design. They found clomipramine to be superior and postulated a specific antitrichotillomaniac effect. They also reported positive responses of two patients treated with fluoxetine. Case reports (22) have noted relapses of patients after 7 weeks to 3 months of treatment with clomipramine, although many of the patients of Swedo et al. maintained their responses at 4- to 6-month follow-up (23).

We conducted a double-blind, placebo-controlled crossover study of fluoxetine in outpatient adult chronic hair pullers and predicted that fluoxetine would be superior to placebo.

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The authors thank Joni Jensen, B.A., for conducting diagnostic interviews and Marguerite Huber, R.N.P., for performing physical examinations.

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METHOD

Subjects were recruited from responders to a newspaper advertisement announcing "a study investigating the treatment of chronic hair pulling with a new medication" and from patients seeking evaluation at the University of Minnesota trichotillomania clinic. Subjects met the following inclusion criteria: 1) they were 18 years of age or older, 2) they were currently engaging in hair-pulling episodes at least three times per week and had done so over the preceding 3 months, 3) they had visible hair loss because of the hair pulling, 4) they were not taking psychotropic medications, 5) they were not currently participating in other psychiatric treatments, and 6) they had had no prior treatment with fluoxetine. The subjects did not have to fulfill *DSM-III-R* criterion B or C for trichotillomania, since previous work with this population (2) had shown that 17% of chronic hair pullers failed to fulfill these criteria (tension before and relief/gratification after pulling hair from the primary site). The presence of psychotic disorders or a psychiatric condition requiring immediate intervention served as exclusion criteria, as did medical conditions precluding safe treatment with high doses of fluoxetine and unwillingness of females of child-bearing age to take precautions against pregnancy.

Eligible subjects underwent an initial 90-minute semistructured interview, the Minnesota Trichotillomania Assessment Inventory (2), which solicited data on demographics and hair-pulling behavior, as well as the National Institute of Mental Health Diagnostic Interview Schedule (DIS) (24), version IIIa. The subjects underwent physical examinations and had ECGs, and all gave written informed consent.

Five measures were used to assess severity of hair pulling throughout the study and served as dependent variables to assess outcome: 1) number of hair-pulling episodes per week, 2) estimated number of hairs pulled per week, 3) counted number of hairs pulled per week, 4) weekly subject rating of severity of the urge to pull out hair, and 5) weekly subject rating of the severity of hair pulling. The subjects were given hair-pulling diaries with instructions to carry these with them throughout the day and to check each time a hair-pulling episode occurred. At the end of each day, they entered an estimate of the number of hairs pulled that day. The subjects also carried envelopes, changed daily, in which they were to collect all hair pulled. They were instructed not to count the hairs to produce their daily estimates of hair loss. The diaries and envelopes were collected at weekly visits; collected hair was counted by the investigators. Daily episodes of hair pulling, estimates of the number of hairs pulled, and hair counts were totaled for each week to be used in the statistical analyses. Subjects were asked at each visit to rate from 0 (none) to 10 (severe) both the urge to pull hair and the severity of hair pulling during the preceding week.

The subjects initially underwent a 1-week assessment of baseline hair pulling. Subjects who pulled hair fewer than three times during the baseline week were dropped from further participation.

Following baseline assessment, subjects were randomly assigned in double-blind fashion to 6-week trials of either fluoxetine or placebo followed by a 5-week washout period before crossover to the other treatment. Placebo and 20-mg doses of fluoxetine were prepared in identical capsules. Within each 6-week treatment period, subjects took one pill per day for 2 weeks, two pills per day for 2 weeks, and four pills per day for the final 2 weeks. The 24-item Hamilton Rating Scale for Depression (25) was administered at the beginning and end of each treatment phase, and the Beck Depression Inventory (26) was completed by the subjects at the beginning and at 2-week intervals during each treatment phase. Subjects were asked to report any physical symptoms or side effects at each visit.

Baseline data indicated great patient variation on the measures used to assess treatment outcome. Given the small sample size, a power analysis was conducted to determine what magnitude of effect would be detectable at a power of 80%. For subject severity ratings of hair pulling and the urge to pull hair, reductions of approximately 40% when taking the active drug, compared to placebo, would be necessary. For the number of hair pulling episodes per week and the estimated hair loss per week, a reduction of approximately 80% when taking the active drug, compared to placebo, would be necessary. All data from weeks 1 through 6 were incorporated into the analyses to increase the likelihood of identifying meaningful trends in the response measures.

Dependent outcome variables were analyzed with a two-way repeated measures analysis of variance, with drug (placebo or fluoxetine) as one repeated variable and experimental period (baseline and weeks 1 through 6) as the other repeated variable.

Thirty-four potential subjects were seen for initial interview after they responded to the newspaper advertisement. Of these, 14 agreed to participate and 20 declined, the majority of the latter citing the inconvenience of the length of the study or the need for weekly visits. Seven additional subjects were recruited from the trichotillomania clinic. These 21 subjects (20 female and one male) completed all interview procedures; however, four subjects were dropped before they entered the treatment phase—two after hair pulling resolved during baseline assessment, one after worsening depression necessitated psychiatric intervention, and one after she found it too emotionally disturbing to monitor hair pulling. The data from an additional subject were excluded from analysis, since insufficient data were available because of several failed appointments. This subject reported complete resolution of hair pulling on day 2 of her placebo regimen, which was maintained 2 weeks into the fluoxetine treatment period, at which point she was dropped from the study.

RESULTS

The sex, age, hair-pulling sites, age at onset of hair pulling, and DIS diagnoses of the remaining 16 subjects

TABLE 1. Clinical Characteristics of 16 Patients With Trichotillomania Who Completed Trials of Fluoxetine and Placebo

Subject	Sex	Age (years)	Hair-Pulling Site	Age at Onset (years)	DIS Diagnosis
1	F	35	Scalp	15	History of major depression and generalized anxiety disorder
2	F	41	Lashes, brows	8	None
3	F	22	Scalp, lashes	11	History of major depression and social phobia
4	F	32	Lashes, brows	23	Generalized anxiety disorder; cannabis abuse; tobacco use disorder
5	F	22	Scalp	5	History of major depression (recurrent) and simple phobia
6	F	33	Lashes	17	None
7	F	33	Scalp	4	History of alcohol and amphetamine abuse/dependence; agoraphobia; generalized anxiety disorder; anorexia nervosa
8	F	28	Scalp	21	History of major depression (recurrent) and generalized anxiety disorder; tobacco use disorder
9	F	34	Scalp	18	History of major depression
10	F	32	Scalp	19	None
11	M	45	Brows, lashes	25	Tobacco use disorder
12	F	27	Brows, lashes, arms	11	None
13	F	25	Scalp, brows, lashes	14	Dysthymia; history of bulimia nervosa, social phobia, and major depression
14	F	28	Scalp, lashes, brows	12	Major depression (recurrent); tobacco use disorder; history of alcohol abuse/dependence
15	F	34	Scalp	15	Major depression (recurrent); generalized anxiety disorder
16	F	35	Brows, lashes	9	History of bulimia nervosa

are presented in table 1. Fourteen subjects met the full *DSM-III-R* criteria for trichotillomania, and two subjects fulfilled all criteria except criterion C, as hair pulling failed to produce a sense of relief or gratification. The mean±SD age of the 16 subjects was 31.6±6.2 years, and the mean±SD duration of hair pulling was 17.0±6.7 years (range=7–33 years). Of these 16 subjects, eight received fluoxetine first and eight were treated initially with placebo. Fifteen completed the study; one female subject was withdrawn from further participation 2 weeks before completion after she developed urticaria while on the fluoxetine regimen. Her data are included in the analysis.

Data on four outcome variables—1) hair-pulling episodes per week, 2) estimated amount of hair pulled per week, 3) weekly subject rating of severity of the urge to pull hair, and 4) weekly subject rating of severity of hair pulling—are presented in figure 1 for baseline and for the 6 weeks of each treatment phase. The data for the one subject who dropped out at week 4 of fluoxetine treatment are included, with data at week 4 carried over to the end-point analysis. The fifth outcome variable, hair counts, was not analyzed, since hair collection proved too sporadic because of the inconvenience (e.g., hair pulling occurring in the workplace or while driving) and the practice of some subjects of ingesting their hair.

The mean±SD scores on the Beck Depression Inventory for the placebo phase were 3.9±2.6 at baseline and 2.9±3.0 at week 6; for the fluoxetine phase the scores were 3.0±2.9 at baseline and 2.4±2.6 at week 6. The mean Hamilton depression scores for placebo were 4.9±3.4 at baseline and 3.6±3.8 at week 6; for fluoxetine the scores were 3.4±4.5 at baseline and 4.4±4.0 at week 6.

No significant Drug by Period interactions were found between baseline and week 6 in regard to number of hair-pulling episodes per week ($F=0.63$, $df=1$, 15 , $p=0.44$), estimated amount of hair pulled per week ($F=0.08$, $df=1$,

15 , $p=0.79$), weekly subject rating of hair pulling ($F=0.08$, $df=1$, 15 , $p=0.78$), or weekly subject rating of the urge to pull hair ($F=0.03$, $df=1$, 15 , $p=0.86$). No significant Drug by Period interactions were noted in regard to scores on the Beck inventory. A weak but significant Drug by Period interaction was noted for the Hamilton depression scores, with improvement in depression noted during the placebo phase and worsening of depression during the fluoxetine phase ($F=5.13$, $df=1$, 15 , $p=0.04$). Mean Hamilton depression scores before and after both treatments were less than 5, well below the threshold for clinical depression.

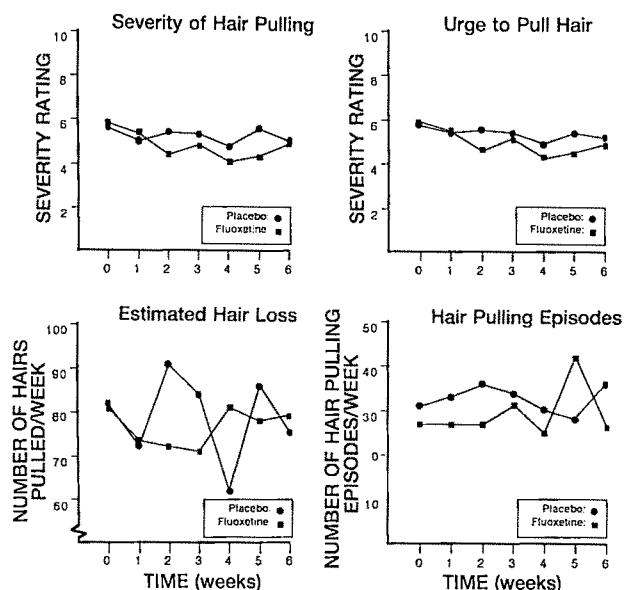
Data from weeks 1 through 6 (figure 1) were analyzed in an attempt to identify meaningful trends in the response measures. No significant Drug by Period interactions were found with regard to weekly subject rating of hair pulling ($F=0.75$, $df=6$, 10 , $p=0.62$), weekly subject rating of the urge to pull hair ($F=0.45$, $df=6$, 10 , $p=0.83$), number of hair-pulling episodes per week ($F=1.41$, $df=6$, 10 , $p=0.30$), or estimated amount of hair pulled ($F=0.29$, $df=6$, 10 , $p=0.93$).

Only the one subject who experienced urticaria had side effects necessitating discontinuation of the drug. Side effects reported for fluoxetine included nausea ($N=5$, 31.3%), tremor ($N=2$, 12.5%), insomnia ($N=2$), dry mouth ($N=2$), urinary hesitancy ($N=2$), irritability ($N=2$), sedation ($N=2$), hot flashes ($N=1$, 6.3%), yawning ($N=1$), anorgasmia ($N=1$), and sweating ($N=1$). Placebo treatment was associated with reports of insomnia ($N=4$, 25%), nausea ($N=2$), diarrhea ($N=1$), headache ($N=1$), lightheadedness ($N=1$), irritability ($N=1$), and irregular menses ($N=1$).

DISCUSSION

Contrary to our expectations, fluoxetine failed to improve hair-pulling behavior when compared to placebo.

FIGURE 1. Mean Weekly Outcome Measures for Trials of Fluoxetine and Placebo in 16 Patients With Trichotillomania



These results are surprising in light of the apparent effectiveness of fluoxetine in open trials (19–21). Several factors may help explain the negative findings.

Our small sample size may have precluded detection of significant differences between fluoxetine and placebo. Examination of individual response patterns revealed that two subjects had complete or nearly complete resolution of hair pulling at the end of the fluoxetine treatment period, suggesting that certain patients may benefit. These responses, however, were balanced by the responses of other subjects who showed no difference in results with the two agents or whose condition worsened when they were taking fluoxetine.

As we have mentioned, at a power of 80%, this study would have failed to detect statistical differences unless a 40% greater reduction in severity of hair pulling or the urge to pull hair or an 80% greater reduction in estimated hair loss or number of hair-pulling episodes occurred during active drug treatment than during the placebo phase. The possibility of a type II error, therefore, needs to be emphasized. Figure 1, however, demonstrates that subjects failed to make clinically meaningful improvements when taking either fluoxetine or placebo, and changes in dependent variables were far short of those necessary to show statistically significant differences.

A potential treatment effect of fluoxetine might have been obscured because we studied a heterogeneous group of hair pullers. For example, different sites of involvement might reflect different pathological processes, with associated differences in treatment response. Ten of our subjects pulled hair primarily from the scalp, whereas the other six pulled eyelashes and eyebrows. Involvement of different sites also adds to interpatient variability with respect to certain outcome variables, since fewer episodes and less hair pulled will result in

more visible hair loss for subjects who pull eyelashes and eyebrows than for those who pull scalp hair. Ratings of severity of hair-pulling urges and ratings of severity of hair pulling would not be expected to have the same limitations, however. It should be noted that studies combining hair pullers who vary in hair-pulling sites may still reveal significant differences in response, as was demonstrated in the study by Swedo et al. (16) comparing clomipramine with desipramine, in which five subjects pulled only eyelashes and eyebrows.

Although several investigators have suggested a relation between trichotillomania and obsessive-compulsive disorder (16, 27), which would imply potentially similar responses to serotonin reuptake blockers, others have thought that trichotillomania is best considered a habit (28). Our experience with more than 120 hair pullers suggests that, although some patients describe intrusive thoughts about pulling out hair and nearly all report some attempts to resist the behavior, the majority say that their hair pulling occurs with little attention focused on it, while they engage in other (usually sedentary) tasks. This is not characteristic of obsessions or compulsions; therefore, trichotillomania may be a heterogeneous disorder, with some cases belonging to an obsessive-compulsive spectrum and others being more habitual in nature.

Differences in subtypes might also be related to severity. For example, severe hair pulling might represent more compulsive pulling, whereas less severe hair pulling might represent a more habitual process. Although some of our subjects had severe cases, others demonstrated milder, patchy hair loss. Differences in severity could also account for the failure to demonstrate a drug effect, as less severe hair pulling would predict less potential for improvement. Examination of individual response patterns, however, revealed that this apparently did not play a role in our study.

Since fluoxetine has antidepressive effects, the affective state of study subjects is an important variable. Two subjects were diagnosed with the DIS as having major depression and one as having dysthymia, although these subjects were not diagnosed as having depression by clinical interview, and their Beck inventory and Hamilton depression scale scores were not in the depressive range. The mean Beck and Hamilton depression scores were below the threshold for clinical depression throughout the study. Only the Hamilton depression scores showed a Drug by Period interaction, but it was in the opposite direction of that predicted: depression scores improved when the patients were taking placebo but worsened when they were taking fluoxetine.

Hair pulling was associated with extreme variability throughout the study, which accounts for the large standard deviations in measures of outcome. Future studies of treatments of trichotillomania should take the high variability in hair pulling into account. We suggest using longer baseline and study periods than those in our study so as to account better for variable patterns of hair pulling over time. Longer treatment phases might also allow for better detection of treatment re-

sponses, as it is unclear when a potential antitrichotillomanic effect should be evident. The 6-week length of our study, however, was comparable to that necessary to detect antidepressant and antiobsessional effects of fluoxetine (29–31). Several studies have demonstrated continued improvement in depressed and obsessive-compulsive disorder patients beyond 6 weeks (30, 32); in one study (30), patients with obsessive-compulsive disorder showed continued improvement at 5 months. Antitrichotillomanic effects were evident within 6 weeks in two of three open studies for which data were recently presented (19, 20); in the third study (21), eight of 10 patients who completed a 3-month trial of fluoxetine, 80 mg/day, demonstrated more than a 60% reduction in hair pulling behavior by month 2, although it is unclear whether improvement was noted before 2 months. A longer trial of fluoxetine may be necessary to demonstrate antitrichotillomanic effects, although, as shown in figure 1, our weekly assessments failed to detect even a trend toward improvement at 6 weeks. Further studies should include treatment periods of at least 8 and possibly 12 or more weeks.

A longer washout period between fluoxetine and placebo phases in studies of trichotillomania should also be considered, as fluoxetine has a half-life of 2–7 days, and its chief metabolite, norfluoxetine (also active), has an average half-life of 7 days (33). One of our fluoxetine responders demonstrated an apparent drug effect that carried over into the placebo treatment phase. This would not alter the conclusions of this study, however, since such a carryover effect would be predicted to add to any apparent fluoxetine effect when compared to placebo.

The dose of fluoxetine we used may have been too low. This seems unlikely, however, as 15 of 16 subjects were treated with fluoxetine for 6 weeks, at a dose of at least 40 mg/day for 4 weeks and a dose of 80 mg/day for 2 weeks. The other subject was treated with fluoxetine for 4 weeks, with the last 2 weeks at 40 mg/day. It has been suggested that higher doses (60–80 mg/day) are more effective in treating obsessive-compulsive disorder (34). Alternatively, the dose may have been too high, with insufficient duration of treatment at lower doses. For depression, one study has shown fluoxetine treatment to be effective with as little as 5 mg/day (35). The optimal dose appears to be 20–40 mg/day (36); higher doses are associated with greater side effects and decreased efficacy (36, 37).

Recently reported open studies have suggested that fluoxetine in both low and high doses may be beneficial in the treatment of trichotillomania. Stanley et al. (19) noted more than a 50% reduction in hair pulling in two of three subjects with trichotillomania by week 1 of treatment with 20 mg/day of fluoxetine; all three patients maintained improvement in hair pulling following an increase of the dose to 80 mg/day at the end of week 2, although two of the three experienced an exacerbation in symptoms between weeks 6 and 12. Winchel et al. (20) treated 13 patients with up to 80 mg/day of fluoxetine (mean dose not specified) and

noted that symptoms of trichotillomania were effectively reduced, with a mean onset of response at 4.1 weeks in a 16-week trial. Benarroche (21) reported a positive response in 10 subjects with trichotillomania who were treated with 80 mg/day of the drug.

It is unclear what the best outcome measurements for detecting improvements in trichotillomania should be. Visible changes in hair growth would be the optimal measure, since it is this complication of hair pulling that seems to cause the most distress for patients and is most readily monitored by observers. Quantification of hair loss could be accomplished by directly measuring patches of hair thinning or baldness and then calculating the surface area involved (38). Although this would suffice for some hair pullers, the common pattern of irregular patches of hair loss and frequent changes of hair-pulling sites in trichotillomania patients suggests that this method might be impractical in large series of subjects. Another method worth consideration is photographing involved areas before and at the end of drug trials and blind rating of severity. These measurements would necessitate long experimental periods, however, since regrowth of hair lags behind cessation of hair pulling, and at times hair loss might even continue for some time after termination of hair pulling through telogen effluvium (1) (in which repeated trauma to the scalp leads to mass movement of hairs into a dormant phase and subsequent falling out of these hairs).

In this study we attempted to use several different measures as outcome variables, including direct patient monitoring of hair-pulling episodes, patient estimates of hair pulled, hair collection, and weekly ratings of the urge to pull hair and actual hair pulling. The last two measures have some resemblance to measures that have been used in monitoring the symptoms of obsessive-compulsive disorder (39) in that they are more global estimates of functioning, whereas the other measures require specific daily attention to and recording of behavior—techniques that have been useful in studies of other behavior disorders such as bulimia nervosa (40). It is currently unclear which outcome variables will prove to be the most useful in monitoring hair-pulling behavior, although this should be one focus of future research in trichotillomania.

In conclusion, we failed to find a therapeutic advantage of fluoxetine over placebo in the treatment of trichotillomania. Further studies of the treatment of this disorder are clearly indicated, especially in light of the conflicting data from recently reported open trials of fluoxetine (19–21) which suggest that this drug may be an effective treatment for hair pulling, and the demonstration by Swedo et al. (16) of the efficacy of another serotonin reuptake blocker, clomipramine, in a double-blind, controlled study of trichotillomania.

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Media Distortion of the Public's Perception of Recidivism and Psychiatric Rehabilitation

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***Objective:** The public's perception about the success or failure of psychiatric rehabilitation is frequently dependent upon information received through the news media. The primary objective of this report is to present an example of how the news media can distort public perceptions of treatment outcome. **Method:** Verbatim quotations were presented from a television news series that alleged criminal recidivism by nine patients purportedly treated for various paraphilias at a large, community-based sexual disorders clinic. Brief case vignettes about each of the nine were then reviewed. This allowed for comparisons between what the media had alleged and what had actually occurred. **Results:** Two of the nine cases were relatively minor instances of recidivism involving no genital contact, although the media presentation had either failed to report this or had suggested otherwise. A third case of alleged recidivism involved a patient who was evaluated but never actually treated by the clinic in the community. A fourth patient had refused recommended clinic treatment upon prison release, and a fifth patient had been discharged from treatment at the clinic because of noncompliance years before recidivating. Other cases presented contained additional misleading information. None of the nine cases was reported by the media in the context of a balanced approach that included treatment successes. Clinic staff were constrained from responding publicly to correct certain misinformation because of patient-psychiatrist privilege. **Conclusions:** Inaccurate media presentations about psychiatric rehabilitation that ignore treatment successes and focus only on alleged failures do a disservice to patients, mental health workers, and society at large. (Am J Psychiatry 1991; 148:1572-1576)*

Recent presidential election campaigns have included debates about the potential for rehabilitating criminal offenders. During the presidential campaign of 1988, candidate Michael Dukakis was criticized by George Bush supporters for having signed the parole papers of inmate Willie Horton. Mr. Dukakis did this while he was governor of Massachusetts.

After being paroled, Horton committed a rape in Maryland. Debates about rehabilitation often involve political rhetoric ("My opponent is 'soft on crime'"), with much verbiage and few data. Criminal behavior is frequently depicted as though it were unidimensional. Psychiatric morbidity, if present, is rarely discussed thoughtfully, and isolated examples of criminal recidivism taken out of context may be presented as "proof" that rehabilitative efforts are useless.

By virtue of their psychopathologies, paraphilic patients can be at heightened risk of committing particular sorts of sexual offenses (1). These can include public exhibitionism, sex with children, voyeurism, frottage, and rape. It is important that clinician-researchers involved in the care of paraphilic patients document long-term treatment outcome, since treatment failure can

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cause distress or injury to innocent persons. Treatment successes rarely receive public attention; failures can become news headlines, possibly in a distorted and misleading fashion. Furby et al. (2) recently surveyed the professional literature on sex offender recidivism, summarizing crucial issues.

The primary purpose of this paper is to present an example of how the news media can distort public perceptions of treatment outcome. It is our contention that these types of distortions can mislead the public, thereby creating a climate of opinion that is unjustifiably biased against psychiatric care. This can lead to faulty public policy decisions and to deprivation of access to potential rehabilitative efforts for some who might be expected to profit from them.

ACTUAL RECIDIVISM VERSUS PUBLIC PERCEPTION

The Johns Hopkins Sexual Disorders Clinic specializes in the treatment of paraphilic disorders. More than 2,000 patients have been evaluated at the clinic over the past 10 years. Several hundred have been offered treatment while residing in the community. The overall 5-year criminal recidivism rate for sexual offenses among more than 600 treated pedophiles, exhibitionists, and sexual aggressors against women has been less than 10% (3). None of the treated exhibitionists ($N > 100$) have become rapists. Criminal sexual recidivism for treatment-compliant pedophiles ($N > 170$) has been less than 3%.

In May 1990 a prominent, publicly known figure from Washington, D.C., referred himself to the clinic for treatment. Because of his position of prominence and respect in the community his admission to a sexual disorders clinic, and the reasons that had necessitated it, quickly became front-page news both locally and nationally (4). While this patient was hospitalized, a Washington, D.C., television station decided to do a series about the Hopkins clinic. Because of concerns that this story might be improperly linked to his admission, and for other reasons discussed later in this paper, clinic representatives declined to be interviewed for the series at that time. The possibility of a later interview was left open.

Following are verbatim quotations from that series about alleged criminal recidivism by nine clinic patients. The television presentation used actual names. These have been deleted here, and in some cases the order of presentation may have been altered to protect patient privacy. The name of the clinic director (the first author of this paper) has also been deleted in some of the following quotations. Additional information is provided after the quotations; this information puts the data presented to the public by the media into a very different perspective. The television commentator stated,

Ann knows from personal experience. Her children were molested not once, but twice. Both times by men [patient 1

and patient 2] who were treated . . . [at the clinic]. There were others like them. While a patient, . . . [patient 3] sexually abused three boys. While an outpatient, . . . [patient 4] allegedly molests a 9-year-old girl. Former . . . [clinic] patient, . . . [patient 5] is convicted for having sexual relations with five boys, ages 7 to 13. While in treatment . . . [patient 6 and patient 7] sexually abused three boys. In April of 1987 . . . [patient 8] accosts and molests seven women in what the papers called a bizarre sex spree. A convicted child abuser, . . . [patient 9] takes two preteenaged boys with him to the . . . [clinic]. While he is in therapy, they drive his car into the wall of the hospital . . . [This patient, patient 9] was later charged with molesting two boys.

In another part of the television series, the commentator stated,

When therapy for a child molester fails, more children are victimized and we found that . . . The Johns Hopkins Sexual Disorders Clinic has had many, many fail. Dr. Berlin (the clinic director) would not talk to us for this series . . .

ADDITIONAL INFORMATION

Patient 1 was a man with a diagnosis of homosexual pedophilia. No details were given in the television presentation to the public about either degree or type of alleged recidivism. This was so even though much of this information was publicly accessible. A review of police reports and charging documents revealed that one of three boys had tossed mulch down the pants of patient 1 in a public playground area. The three youngsters stated that patient 1 then put mulch down their pants. None of the boys alleged genital or sexual contact. One of the boys stated that the patient, who had a young son himself, had repeatedly refused requests to give him motor scooter rides. In the past the patient had offended by fondling boys on his scooter. The police investigation into this matter had been initiated after a parent-teacher association meeting at which a parent disclosed that "there was a convicted child molester living in the community." Upon the advice of his public defender, patient 1 pleaded guilty to a minor offense against each of the three boys in question.

Patient 2, accused of "molesting" several boys, either was never seen at the clinic (no identifying information was given other than his name) or was briefly hospitalized (for approximately 3 weeks) about 5 years earlier in a medical/psychiatric consultation for a second opinion. At no time was patient 2, who resided in New York rather than Baltimore (where the clinic is located) at the time of his referral, actually treated by the clinic in the community. During his hospitalization the patient declined to follow the clinic's recommendation that he take testosterone-lowering medication to reduce his paraphilic urges.

Patient 3, a business professional with a diagnosis of homosexual pedophilia, was a treatment failure. He received three consecutive 18-month sentences secondary to sexual activity with boys.

Patient 4, who allegedly "molested a 9-year-old girl,"

was mentally retarded. He had a history of several other psychiatric impairments as well, including attention deficit disorder with hyperactivity, and paraphilia. He had spent many years in a facility for retarded individuals before being released into the community. He had little family support. The clinic had considered him to be a high-risk patient, but because at the time of clinic referral he had free access to the community, a decision was made to try to work with him. Although considered high risk, he was not psychiatrically committable under the standards of "immediate danger to himself or others." Indefinite preventive detention for a crime he might someday commit was not legally permissible. A number of letters had been sent, however, by clinic staff to the program manager of adult protective services and to the director of the mental hygiene administration emphasizing the urgent need to provide this limited individual with additional structure and support. Those letters cautioned, "we hope you will pursue this case with some urgency to prevent a potentially tragic outcome." Unfortunately, such support was not forthcoming. When, as had been feared, he did relapse, the court ruled that he was not competent to assist in his own defense. He was not incarcerated, but instead was placed in a mental health facility for retarded persons.

Patient 5, convicted for having sexual relations with five boys, had been discharged from the clinic several years earlier for noncompliance. This occurred after he had refused to accept recommended treatment. For this reason the clinic had declined a request to consider him for additional treatment in the community after his subsequent arrest.

Patient 6, a young man with a diagnosis of homosexual pedophilia, had initially been treated at the clinic as a condition of probation a number of years before the recidivism referred to by the television commentator. Another condition of his probation had been that he avoid all unnecessary associations with youngsters. That probation was violated after he was seen playing ball with children in the streets of his neighborhood.

At the time of his hearing on the probation violation, clinic staff recommended to the court that at least part of his sentence remain suspended. This was so that there could be leverage, once again requiring treatment as a condition of probation upon his reentry into the community. The court declined to follow that advice.

Patient 6 did receive some treatment in prison, but he refused follow-up upon reentry into the community. Throughout his incarceration he insisted that he did not believe sex with boys was wrong. He continued to view boys in a sexualized, romantic, loving way. For this reason he was considered to be at very high risk of eventual recidivism. Repeated unsuccessful efforts were made to persuade him to accept help after his release. He was not considered an immediate danger to himself or others and therefore was not psychiatrically committable (although in the past, clinic staff had committed him against his will when the degree of immediate risk to others had appeared more imminent). Tragically, his eventual recidivism came as no surprise to clinic staff,

who had tried repeatedly but unsuccessfully to engage him in treatment.

Patient 7, who relapsed by also having sex with a number of boys, had initially entered treatment at the clinic at a time when he was living in the community. Patient records reveal that his prognosis was consistently considered "poor" by clinic staff. However, because he was free in the community, having been placed on probation before referral to the clinic, a decision was made to try to work with him. This seemed reasonable, since the patient was living in the community and attempting to treat him was certainly not going to increase public danger. The patient, a professional person, had a lengthy history of soliciting adolescent boys for sex. The discharge summary from his initial inpatient hospitalization read, "This hospitalization confirmed his previous outpatient assessment of his being a patient with high risk of reoffending." In response to a letter from the sentencing judge following a later arrest, clinic staff indicated that unfortunately, they did not feel confident about their ability to treat this man successfully in the community at that time. Instead, they recommended treatment at a local prison-based rehabilitation program.

Patient 8, accused in the television newscast of accosting and molesting seven women, was a man with a diagnosis of manic-depressive illness and paraphilic disorder as well. Before entering treatment at the clinic, he had committed a number of sexual offenses, including rape. Contrary to the allegations in the newscast, he was not charged with any new sexual offenses while in treatment. Although the television commentator quoted a newspaper story describing patient 8's behavior as a "bizarre sex spree," he made no mention whatsoever of a subsequent newspaper article whose headline had read, "[Patient 8's] case has the look of a failure, but closer inspection shows it isn't" (5). Patient 8 had gone around in broad daylight in a frenzied state, spraying some type of aerosol substance in the direction of several different women. None of the women was sexually assaulted or injured in any way whatsoever. He pleaded guilty to two misdemeanors and was placed back on probation but was given no jail time. He has done remarkably well ever since—a period of approximately 4 years. Single and unemployed at the time he entered treatment, he is now married with two children and is a successful businessman.

Patient 9, an elderly man with a diagnosis of homosexual pedophilia, was initially treated at the clinic many years before the recidivism referred to by the television commentator. He had then gone to prison secondary to a violation of probation. That violation came about after clinic staff reported to his probation officer that he was not complying with treatment.

Subsequently, the patient was paroled. Because he was free again in the community, a decision was made to try to help. Clinic staff initiated an investigation through child protective services when staff became concerned that he might be using his young daughter as a means of recruiting boys for sexual activity. That in-

vestigation found no evidence of abuse or neglect. When clinic staff learned that he was continuing to spend an inordinate amount of time with two young boys in spite of their mothers' knowledge of the patient's background, they insisted that the youngsters be brought to the hospital so that they could be interviewed. At that time the boys vehemently denied any sexual contact with the patient. Staff had been prepared to report the patient to legal authorities had these youngsters made any allegations. The patient's eventual arrest was not unexpected.

DISCUSSION

Only a small percentage of patients at the sexual disorders clinic (less than 5% among those who have complied with treatment) have been subsequently charged with a repeated sexual offense over an average 5-year follow-up period (3). Furthermore, some of that recidivism has been relatively minor. Data currently being analyzed for longer-term follow-up appear similarly promising. If 90% of patients are treated successfully, for every 90 successes there will be 10 failures. If the media chooses to present failures out of context and in a distorted fashion, the public can be left with a false impression about psychiatric treatment and rehabilitation.

This paper presented an example of nine cases listed by the media as treatment failures. In each case there was some truth to the media presentation. However, as summarized in table 1, more substantive analysis revealed the presence of substantial misleading information. Other points made in the news series in question were often similarly distorted. For example, the commentator made reference to yet another patient named "Tony." He described Tony as "a sexual deviant" and a man who had "sexually attacked women." This was a man who developed a paraphilic disorder and began having difficulties with sexual impulses only after sustaining severe brain injury in a motor vehicle accident that had left him comatose for weeks. Subsequently, he was left with obvious neurological impairment including a severe gait disturbance. His inappropriate sexual advances had been readily repelled by women whom he approached after the injury. Often it was what the media had failed to say that was just as important as what had been reported.

One could argue that the media report in question might have been more balanced had clinic staff been willing to grant the requested interview. The clinic director would ordinarily have been willing to do so, and indeed in the past has granted media interviews on a number of occasions. However, in this particular instance he was advised against this by colleagues because of several important concerns.

First, it seemed clear after preliminary conversations with the news commentator in question that the bulk of his report (which was to run as a series over the course of 3 or 4 days on the evening news) had

TABLE 1. Clinical and Behavioral Data on Nine Men Allegedly Treated for Paraphilias Who Were Reported in the Media to Be Recidivists

Patient	DSM-III-R Diagnosis	Media Statement	Comment
1	Homosexual pedophilia	Molested children	No genital contact alleged
2	Homosexual pedophilia	Molested children	Evaluated in hos- pital; refused treatment rec- ommendations; not treated by clinic
3	Homosexual pedophilia	Sexually abused three boys	
4	Mental retarda- tion, attention deficit disorder, paraphilia not otherwise specified	Allegedly mo- lested 9-year- old girl	Found not com- petent to stand trial
5	Homosexual pedophilia	Had sexual relations with five boys	Discharged for noncompliance with treatment years before recidivism
6	Homosexual pedophilia	Sexually abused three boys while in treatment	Not in treatment at that time; repeatedly re- fused to accept treatment be- fore recidivism
7	Homosexual pedophilia	Sexually abused three boys while in treatment	
8	Manic-depressive illness, para- philia not other- wise specified	Accosted and molested seven women	Molested no women
9	Homosexual pedophilia	Took boys to clinic, molest- ed two boys	Boys taken to clinic for evalu- ation at clinic request

already been filmed and prepared well before clinic staff had even been contacted. Thus, clinic staff were being afforded an opportunity to respond after the fact in a way that almost certainly would have seemed defensive. In addition, the opportunity to respond was in such a fashion that videotaped answers could be edited and possibly presented out of context. In fact, when the series was ultimately aired, videotaped excerpts of comments made by the clinic director at other times and about other issues indeed were taken out of context.

Hospital colleagues also had some reservations about the professional propriety of engaging in a media "debate" over matters perhaps better addressed through publications in peer-reviewed journals. An "ivory tower" approach that precludes responding to legitimate community concerns through the media, however, needs also to be avoided.

More important than these issues in deciding not to grant a media interview in this particular instance were concerns about protecting confidential information about patients. As already noted, the television com-

mentator referred to numerous patients by name. In order to correct misinformation about these individuals it would have been necessary in some instances to reveal privileged clinical details, including details about non-compliance with treatment. To do so would have been unacceptable medical practice. The requirement that psychiatrists must maintain patient privilege can pose a substantial, albeit necessary, handicap when the need to honor that commitment inhibits the correction of false public perceptions. This has been a dilemma for the clinic on other occasions in the past as well.

Although it is our belief that the news media generally attempt to be objective and fair, it can also sometimes respond to perceived public sentiments and interest groups. There are many advocacy groups in contemporary society that argue for "tougher treatment of criminals," that feel that "too little is done for victims and too much for offenders," and that believe that psychiatrists "excuse sin" by relabeling it psychopathology (6, 7). Those who hold such views are often cynical about treatment and rehabilitation. They may also polarize public opinion by characterizing offender treatment as competitive with victim assistance, rather than as an aspect of primary prevention.

When it comes to psychiatric disorders such as pedophilia and some of the other paraphilias that can predispose those afflicted toward criminal behavior, there has been little effective professional advocacy supportive of treatment. Few psychiatric facilities, research institutions, or residency training programs target this group of disorders. In response to a recent letter from the mother of an incarcerated pedophile, syndicated columnist Ann Landers recommended a self-help organization called Molesters Anonymous (8). Apparently the public has little knowledge about how to find specialized professional help for these types of disorders. The families of patients afflicted with these conditions may be too embarrassed or fearful of stigma to identify themselves. The patients themselves are often dismissed as "bad" or lacking in credibility. Thus, in some instances at least, and this may have been one, the media may be prone to support the perceived stance of certain victim advocacy groups to the detriment of those providing treatment to paraphilic patients. If the psychiatric profession believes conditions such as the paraphilias are legitimate mental disorders and that some persons are predisposed toward certain criminal acts as a consequence of legitimate psychopathology, then the profession may need to do much more in terms of teaching, research, and clinical care in this area. Otherwise, the relatively few treatment programs currently in exist-

ence may default to public prejudices and unfavorable misperceptions about psychiatric rehabilitation.

Publications in scholarly peer-reviewed journals about long-term outcome can help develop a database supportive of psychiatric treatment. This must be done. However, these types of "academic" data may carry little weight with the public in the face of the strong emotions often elicited when innocent persons suffer at the hands of an individual who has failed in treatment. The suffering and humanity of those afflicted with psychiatric disorders, and the suffering of their families, must also somehow be communicated to the public. Until the news media begins to consider the occurrence of good events, such as successes in treatment, to be as newsworthy as the occurrence of tragedies, the public's perception of psychiatric interventions may continue to remain unfavorably skewed and distorted.

Tragically, with psychiatric disorders such as alcoholism, drug abuse, certain forms of major mental illness, and the paraphilias, which can predispose some of those afflicted toward criminal activity, some recidivism is inevitable. Persons who are incarcerated without treatment also relapse and most such persons, whether sooner or later, will be free in the community. Biased media presentations that focus only on treatment failures, sometimes in a less than fully informed fashion, do a disservice to patients, mental health workers, and society at large. The psychiatric profession may need to take a more active advocacy role in the area of the paraphilias in particular if as a profession it truly believes that issues of diagnosis, treatment, and rehabilitation need to be addressed more objectively and in a more enlightened fashion.

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CT Scan Abnormalities and Outcome of Chronic Schizophrenia

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The authors evaluated the relationship between brain morphological characteristics assessed by means of computerized tomography and the 2-year clinical and social outcomes of 18 patients with chronic schizophrenia. Cerebral structural abnormalities, especially cortical atrophy, were associated with a poorer outcome in several areas of clinical and social functioning.
(Am J Psychiatry 1991; 148:1577-1579)

In recent years computerized tomography (CT) has enabled demonstration of neuromorphological abnormalities in schizophrenia and has proved useful in characterizing groups of patients differing in many clinical and biological variables (1).

Mainly because of difficulties in evaluating it correctly, clinical and social outcome remains one of the least studied variables in relation to neuromorphological characteristics, even though much indirect evidence suggests a possible link between these measures. Lateral ventricle size has been correlated with symptom picture, neuropsychological performance, premorbid functioning, family history of schizophrenia, and treatment response to neuroleptics (1). All of these measures are considered to be predictors of the outcome of schizophrenia (2).

In this study we directly evaluated the relationship between ventricle size and long-term outcome of schizophrenia and between cortical atrophy and long-term outcome of the disorder.

METHOD

All of the patients admitted for the first time to the Schizophrenia Research Center at the Institute of Psy-

chiatry of the University of Milan between January 1988 and March 1988 who fulfilled *DSM-III-R* diagnostic criteria for chronic schizophrenic disorder entered the study and underwent CT scanning of the brain with the use of a GE 9000 II tomograph. This period of time was chosen because all of the patients had had complete clinical and CT evaluation, with no exceptions that could bias the sampling process. All diagnoses were made by two expert psychiatrists before the scans were performed.

Twenty-one patients entered the study. Twelve of these patients were men and nine were women; their age range was 20-45 years.

Cerebral ventricle size, expressed as ventricle-brain ratio (VBR) (3), was measured by two raters who used a manual planimetric method. The interrater reliability was high ($r=0.93$). Cortical atrophy was determined by one rater who used a subjective method based on the width of the cortical sulci and sylvian and interhemispheric fissures with reference to a 4-point scale (0=no atrophy, 1=dubious or mild atrophy, 2=moderate atrophy, and 3=severe atrophy) (4). One patient did not receive a rating of cortical atrophy because of persisting uncertainty of class attribution of the CT picture. The CT raters were blind to the patients' diagnoses and clinical characteristics.

Two years after they entered the study, patients were recalled and their outcome was assessed by means of a structured questionnaire that included the Strauss-Carpenter Scale (5). This scale consists of four subscales rated 0-4: hospital stay, severity of symptoms, useful employment, and social contacts. The patients were

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TABLE 1. Relationship Between Brain Structural Characteristics and Outcome of Patients With Chronic Schizophrenia

Outcome Measure	Ventricular Enlargement (N=18)						Cortical Atrophy (N=17)					
	Present (N=4)		Absent (N=14)		Mann-Whitney U	r_s	Present (N=6)		Absent (N=11)		Mann-Whitney U	r_s
	Mean	SD	Mean	SD			Mean	SD	Mean	SD		
Scores on Strauss-Carpenter Scale												
Severity of symptoms	1.7	1.8	2.4	1.1	20	0.20	2.3	1.7	2.2	1.1	30	0.14 ^a
Useful employment	0.0		1.5	1.6	11 ^a	-0.31	0.0		1.9	1.6	8 ^b	-0.64 ^b
Hospital stay	3.0	1.2	3.6	1.0	20	-0.19	2.7	1.6	3.8	0.4	15 ^a	-0.42 ^c
Social contacts	1.2	1.1	1.8	1.4	18	-0.23	0.8	1.1	2.2	1.3	15 ^a	-0.44 ^c
Total score	6.0	3.2	9.4	3.0	20	-0.40	5.8	2.7	10.2	2.8	9.5 ^b	-0.59 ^d
Score on intimacy of interpersonal contacts scale	0.0		0.8	0.9	12 ^e	-0.21	0.0		1.1	0.9	10 ^f	-0.57 ^d

^ap<0.04.^bp<0.01.^cp<0.10.^dp<0.05.^ep<0.07.^fp<0.02.

also rated 0–4 on the scale for intimacy of interpersonal contacts derived from the standard follow-up interview of McGlashan (6).

It was not possible to obtain outcome ratings for three patients: one had moved to another city and was not found and two, living in the community, refused to be interviewed. The final study group, therefore, consisted of 18 patients. Eleven of these were men and seven were women; their mean age at follow-up was 30.7±7.5 years (range=22–47).

The outcome scales were administered by one rater who was unaware of the nature of the study and of the baseline CT scan measures. The reliability between two raters (one of whom was the rater of this study) of the Strauss-Carpenter scale and the intimacy scale had been measured in a group of 20 subjects by means of the Cohen kappa statistic for the single subscales and by means of a linear regression analysis through axis origin ($y=bx$ as a model) for the total score of the Strauss-Carpenter Scale. The results of these analyses were fairly good to good: for hospital stay, kappa=0.86; for useful employment, kappa=0.83; for severity of symptoms, kappa=0.69; for social contacts, kappa=0.75; for total Strauss-Carpenter score, $\beta=0.94$ (not statistically different from 1); and for intimacy of interpersonal contacts, kappa=0.55.

All patients had taken neuroleptic drugs during the follow-up period. The statistics used were the Mann-Whitney U test and the Spearman rank correlation.

RESULTS

The mean VBR of the 18 patients who completed the study was 5.2±3.7. We considered abnormal any VBR higher than 7.5, which is the mean plus two standard deviations of a group of 80 healthy control subjects matched to our 18 patients for age. Four patients showed ventricular enlargement and 14 had normal ventricle dimensions. Eleven of the patients had no or mild atrophy (scores of 0–1), and six had moderate to severe atrophy (scores of 2–3).

The mean scores on the outcome measures of patients with and without ventricular enlargement or cortical atrophy are shown in table 1. Patients with and without ventricular enlargement showed a significant difference in the employment score; poorer outcome in this area was associated with enlargement (table 1). A trend in the same direction emerged relative to the intimacy scale (table 1). The individual VBR values, however, did not correlate significantly with any of the outcome scale scores (Spearman rank correlation).

Cortical atrophy, on the other hand, significantly differentiated the patients' outcome on five of the six scales, predicting a poor outcome in the areas of useful employment, hospital stay, social contacts, total Strauss-Carpenter score, and intimacy of interpersonal contacts (table 1). On the same scales, there were significant negative correlations between atrophy scores and outcome values: the greater the atrophy the poorer the outcome (table 1). No association was found between cortical atrophy and the severity of symptoms score on the Strauss-Carpenter scale.

In this group of patients, no outcome scale score was significantly affected by patients' age at admission, sex, age at onset, or duration of the disorder (Spearman correlation and Mann-Whitney tests).

DISCUSSION

We found a significant association between CT evidence of brain morphological abnormalities and poor outcome in several areas of clinical and social functioning; cortical atrophy was more "predictive" than ventricular enlargement regarding patients' outcome.

In the light of the multidetermined nature of outcome, which is known to be influenced by social, clinical, and biological factors, we would not expect to find variables that by themselves have a high or "absolute" prognostic value, especially in such a small study group. Further, only multivariate analyses of large patient populations that take into consideration several vari-

ables would be able to determine more conclusively the factors actually responsible for different clinical outcomes. Our results indicate, however, that brain morphological characteristics may be one of these relevant factors. We found that variables such as the patient's age and sex and the duration of schizophrenic illness at the time of the first contact were unrelated to outcome measures, thus excluding their having a relevant weight in determining our results.

The associations found between outcome and CT evidence of atrophy is in line with previous reports. Williams et al. (7) reported greater ventricular dilatation in patients with a bad or intermediate prognosis than in patients with a better outcome. Another remarkable observation was that the percentage of subjects with ventricular dilatation seemed to be significantly different in "chronically hospitalized patients" (8) and "remitting patients" (9). Keefe et al. (10), however, did not find any difference in the absolute values of VBR between patients with "Kraepelinian schizophrenia" and those in remission or those with symptom exacerbation requiring hospitalization, although more of the patients with schizophrenia had ventricular asymmetry.

We are not aware of any study that has evaluated disease outcome in relation to cortical atrophy, but in our study, cortical atrophy proved to be the more important predictive factor for outcome. In fact, it was predictive of outcome in all but one of the areas considered.

It could be argued that the differences in outcome of patients with and without cortical atrophy may reflect differences in baseline or premorbid functioning of these patients. The lack of an initial evaluation of the Strauss-Carpenter and intimacy scales makes it impossible to attribute a pure outcome significance to the differences detected in the scale scores and to exclude a more stable component of worse functioning and adjustment of patients with cortical atrophy. Although this possibility should be specifically addressed, it would contrast with the data indicating that the presence of cortical atrophy seems less important than ventricular enlargement in discriminating schizophrenic

subgroups with specific clinical features. In fact, in a group of 124 schizophrenic patients, patients with and without atrophy could not be differentiated with respect to social functioning (employment), symptoms, response to neuroleptics, or suicidal behavior (4).

The different results detected for patients with and without cortical atrophy in the measures obtained 2 years after admission could indicate the existence of at least a component of poorer long-term outcome in patients with atrophy.

Because of its clinical importance, the prognostic value of brain structural abnormalities in schizophrenia warrants further analyses.

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Correlation of Wisconsin Card Sorting Test Performance With Eye Tracking in Schizophrenia

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The authors studied the relationship between performance on the Wisconsin Card Sorting Test and on the Trailmaking-B test and measures of smooth pursuit eye movements in 12 patients with chronic schizophrenia and 12 normal volunteers. They found that performance on the Wisconsin Card Sorting Test was significantly correlated with measures of smooth pursuit eye movements in schizophrenic patients but not in normal subjects. Trailmaking-B scores, however, were unrelated to smooth pursuit eye movements in either group.
(Am J Psychiatry 1991; 148:1580-1582)

Impaired smooth pursuit eye movement is a psychophysiological deficit found in a substantial proportion of schizophrenic patients (1). Although abnormal smooth pursuit eye movements are postulated to be a genetically determined trait marker in schizophrenia (1), their precise nature and their relationship to the pathophysiology of schizophrenia are largely unknown. Nonhuman primate experiments that suggest the involvement of the prefrontal cortex in mediating both smooth pursuit eye movements and saccadic eye movements (2) raise the possibility that smooth pursuit eye movement abnormalities reflect diminished frontal cortical function in schizophrenia (3).

Studies applying neuro-ophthalmological techniques to quantify smooth pursuit eye movements in order to better define the deficit in schizophrenia have reported low smooth pursuit eye movement gain (eye velocity/target velocity) and more saccades interrupting smooth pursuit eye movements (4). We sought to use quantitative measures to investigate the relationship between abnormal smooth pursuit eye movements and frontal cortical function in schizophrenia. We measured smooth pursuit eye movement gain and saccadic frequency during smooth pursuit eye movements by using infrared oculography and examined their relationship to performance on the Wisconsin Card Sorting Test (5), a neuropsychological test of abstract thinking and ability to shift mental sets that is sensitive to prefrontal cortical dysfunction (6), and the Trailmaking-B test (7), a

neuropsychological test of visual-conceptual and visual-motor tracking sensitive to global brain dysfunction.

METHOD

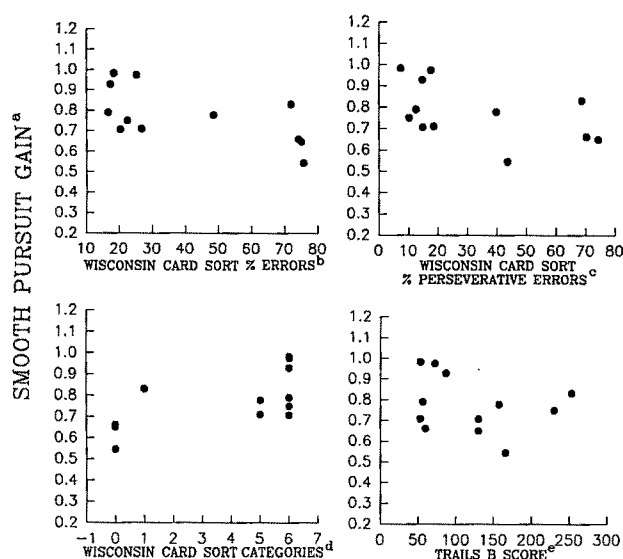
Smooth pursuit eye movements were measured in 12 healthy normal comparison subjects and in 12 schizophrenic patients. The comparison subjects were screened for psychiatric illness by using a structured interview based on Research Diagnostic Criteria (RDC); the schizophrenic subjects were inpatients and outpatients diagnosed according to RDC. These patients had chronic schizophrenia; they had been ill for a mean \pm SD of 11.3 ± 1.1 years, and they had had a mean of 6.6 ± 1.0 previous hospitalizations. The mean age of the comparison subjects was 28.8 ± 5.0 years; that of the schizophrenic patients was 28.0 ± 1.6 years. Eleven of the comparison subjects were men and one was a woman; nine of the schizophrenic patients were men and three were women. All of the comparison subjects and 11 of the schizophrenic patients were Caucasian; one of the schizophrenic patients was black. All patients were medicated with fluphenazine, thioridazine, or haloperidol (their mean dose was 16.9 ± 4.0 mg/day in fluphenazine equivalents) and had been receiving stable doses for 2 weeks or more. Patients differed from normal subjects in that they had less education (12.1 ± 1.8 compared with 16.5 ± 2.1 years; $t=4.95$, $df=22$, $p<0.001$).

Neuropsychological testing was administered to all subjects according to methods described elsewhere (5, 7), within 2 months of the recording of smooth pursuit eye movements.

After informed consent had been obtained, smooth pursuit eye movements were recorded by using infrared oculography during a visual tracking task in which the target moved horizontally at a constant velocity of

Received Dec. 4, 1990; revision received May 3, 1991; accepted June 3, 1991. From the Section on Clinical Studies, Clinical Neuroscience Branch, and the Laboratory of Clinical Science, NIMH; the VA Medical Center, Seattle, Wash.; and the Biomedical Engineering and Instrumentation Branch, NIH, Bethesda, Md. Address reprint requests to Dr. Litman, Section on Clinical Studies, Clinical Neuroscience Branch, NIMH, NIH Bldg. 10-4N214, 9000 Rockville Pike, Bethesda, MD 20892.

FIGURE 1. Correlations of Smooth Pursuit Eye Movement Gain With Wisconsin Card Sorting Test and Trailmaking-B Scores in 12 Patients With Chronic Schizophrenia



^aLow smooth pursuit eye movement gain=poor performance.

^b $r_s = -0.66$, $df = 11$, $p < 0.02$.

^c $r_s = -0.60$, $df = 11$, $p < 0.04$.

^d $r_s = -0.69$, $df = 11$, $p < 0.01$.

^e $r_s = -0.27$, $df = 11$, n.s.

16.67°/second, capturing 30° of visual arc, for a total of 30 seconds. After calibration, subjects were instructed to follow the target as accurately as they could. Smooth pursuit eye movement gain and saccadic frequency (saccades/second) were measured by one of the investigators (R.E.L.) and a research assistant using an interactive computer program that displays eye and target position and velocity on a computer screen, as described elsewhere (8). Smooth pursuit eye movements were identified by visual inspection and were considered to be any interval of eye movement during which eye velocity did not exceed 50°/second. Saccades were discontinuities in eye movement in which velocity exceeded 50°/second. Eye blinks were excluded from measurement on the basis of their distinct morphology. Smooth pursuit eye movement gain was calculated by taking the mean velocity of all smooth pursuit eye movement intervals, adjusted for their duration, and dividing this value by the target velocity. Interrater reliability (intraclass correlation coefficient) for all measures was 0.95 or more.

Percentage of total errors, percentage of perseverative errors, and number of categories achieved on the Wisconsin Card Sorting Test as well as the amount of time (in seconds) to complete the Trailmaking-B test were measured in all subjects. Student's *t* tests, two-tailed, were used for statistical comparisons; the Mann-Whitney *U* test, two-tailed, was used when assumptions for parametric statistics were not met. Spearman rank-ordered correlations of eye tracking

measures and neuropsychological test scores were also performed.

RESULTS

Smooth pursuit eye movement gain was significantly lower in schizophrenic patients (0.78 ± 0.14) than in the normal subjects (0.87 ± 0.07) ($t = 2.22$, $df = 15$, $p < 0.05$), and saccadic frequency was significantly higher in the patients (1.71 ± 0.59 saccades/second) than in the normal subjects (1.04 ± 0.48 saccades/second) ($t = -3.05$, $df = 22$, $p < 0.01$). On the Wisconsin Card Sorting Test, patients had a higher percentage of errors (median=25.9%, range=16.5%–75.8%) than normal subjects (median=12.6%, range=8.6%–20.7%) ($U = 137$, $p < 0.01$) and a higher mean \pm SD percentage of perseverative errors ($32.7\% \pm 25.6\%$ versus $6.3\% \pm 2.9\%$) ($t = -3.55$, $df = 11$, $p < 0.01$). Since all 12 of the normal subjects achieved six categories on the Wisconsin Card Sorting Test, the categories scores of all subjects were divided by the number of trials needed to complete the Wisconsin Card Sorting Test. The normal subjects achieved more categories using fewer trials (median=0.08, range=0.07–0.09) than did schizophrenic patients (median=0.045, range=0–0.08) ($U = 135$, $p < 0.01$). Patients took longer to complete the Trailmaking-B test (120.6 ± 20.1 seconds versus 59.8 ± 4.1 seconds) ($t = -2.96$, $df = 12$, $p < 0.01$).

Smooth pursuit eye movement gain was significantly correlated with Wisconsin Card Sorting Test performance in schizophrenic patients (figure 1). Saccadic frequency was not ($r_s = 0.30$ with percentage of errors, and $r_s = -0.35$ with number of categories achieved). Wisconsin Card Sorting Test scores and smooth pursuit eye movements were unrelated in the comparison subjects. The Trailmaking-B scores of schizophrenic patients were not significantly correlated with smooth pursuit eye movement gain (figure 1) or saccadic frequency ($r_s = 0.25$), but in normal subjects their correlation with smooth pursuit eye movement gain approached significance ($r_s = -0.50$, $p < 0.09$). The correlation between Trailmaking-B scores and saccadic frequency in the normal subjects was not significant ($r_s = 0.28$). Finally, schizophrenic patients' years of education correlated with smooth pursuit eye movement gain ($r_s = 0.63$, $p < 0.03$) but not saccadic frequency ($r_s = 0.13$); no correlations were found in normal subjects.

DISCUSSION

Consistent with previous studies (1, 4, 6), our findings show disordered smooth pursuit eye movements and poor neuropsychological performance in schizophrenic patients. Significant correlations between performance on the Wisconsin Card Sorting Test, which is sensitive to prefrontal cortical dysfunction (6), and smooth pursuit eye movement gain in schizophrenic pa-

tients suggest a functional relationship between abnormal smooth pursuit eye movements and frontal cortical dysfunction in schizophrenia. These variables were unrelated in normal subjects. These data are compatible with lesion experiments of the frontal eye fields, areas of association cortex in the prefrontal cortex, which result in low smooth pursuit eye movement gain (2). The absence of significant correlations between saccades interrupting smooth pursuit eye movements and Wisconsin Card Sorting Test measures may be related to the heterogeneity of saccades during smooth pursuit eye movements, i.e., subtypes of saccades that represent different aspects of cerebral function (4). Subtyping saccades in future experiments might clarify the relationship between frontal cortical dysfunction and high saccadic frequency during smooth pursuit eye movements in schizophrenia.

Inattention or lack of motivation during task performance (6), factors that may not directly relate to frontal lobe function, may have contributed to our findings. However, since these factors are also involved in Trailmaking-B performance, it is unlikely that they alone explain our results. Moreover, since the Trailmaking-B test measures global brain dysfunction (7), low correlations between Trailmaking-B scores and smooth pursuit eye movement measures further support the notion of regionalized cortical dysfunction underlying abnormal smooth pursuit eye movements in schizophrenia.

Even so, it is possible that intellectual ability rather than psychopathology accounts for these observations, especially in view of the fact that patients' years of education correlated with their smooth pursuit eye movement gain. Clarifying this issue would require controlling for intellectual ability in patients, e.g., by using

a comparison group matched in intellectual level. That and the likelihood of type II error given the small size of our study group are limitations that warrant cautious interpretation of these results. Nonetheless, these data suggest a relationship between prefrontal cortical dysfunction and smooth pursuit eye movement abnormalities in schizophrenic patients. Further classification of saccades during smooth pursuit eye movements and their relationship to neuropsychological and other measures of brain function (e.g., positron emission tomography and regional blood flow) in larger, properly designed studies will provide further insight into the pathophysiology underlying smooth pursuit eye movement dysfunction in schizophrenia.

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Higher Lifetime Prevalence of Respiratory Diseases in Panic Disorder?

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Current and past frequencies of respiratory diseases were assessed in 30 patients with panic disorder, 30 patients with obsessive-compulsive disorder, and 30 patients with eating disorders. Lifetime prevalence of respiratory disorders was significantly higher in patients with panic disorder (47%) than in patients with either obsessive-compulsive disorder (13%) or eating disorder (13%). Point prevalences showed no differences.

(Am J Psychiatry 1991; 148:1583-1585)

There is considerable resemblance between the symptoms of panic disorder and some diseases affecting the respiratory system. Dyspnea, choking, and smothering sensations are among the most important features common to both. Anxiety, a predominant symptom of panic disorder, also occurs in asthmatic patients (1), in whom it is considered to be of a secondary nature. Strong evidence exists that disturbances in respiratory control, such as hyperventilation, are common to both panic disorder (2) and asthmatic disorders (3).

This resemblance in symptoms could point to some overlap in pathophysiology, or at least to a relationship between panic disorder and some respiratory disorders. Additional evidence for this comes from recent research on the comorbidity of diseases affecting the respiratory system and panic disorder. Karajgi et al. (4) found that the prevalence of panic disorder was higher in a group of patients with chronic obstructive pulmonary disease than in the general population.

The present study explored the inverse, i.e., the prevalence of respiratory diseases in patients with panic disorder. Past and present frequencies of disturbances in the respiratory tract were assessed in patients with panic disorder and compared with those found in patients with obsessive-compulsive disorder and eating disorders. Our hypothesis was that both lifetime and point prevalences of respiratory diseases would be higher in panic disorder than in either obsessive-compulsive disorder or eating disorders.

METHOD

Data were obtained by means of a retrospective file study. Subjects were chosen from the outpatient files at a psychiatric hospital anxiety center; the 30 most recently referred patients for each group were selected. The first group consisted of 30 patients with panic disorder with or without agoraphobia (11 men and 19 women; mean \pm SD age = 35.5 ± 10.1 years). Two comparison groups were included. One consisted of 30 patients with obsessive-compulsive disorder (11 men and 19 women; mean age = 34.3 ± 10.01 years) and the other of 30 patients with eating disorders (two men and 28 women; mean age = 25.5 ± 5.4 years). All subjects had been diagnosed by experienced clinicians using the criteria of *DSM-III-R*. A full medical history was taken and a complete physical examination was done on each patient.

Point and lifetime prevalences of respiratory disorders (asthma, bronchitis, allergy, pneumonia) were assessed in each group. Since the group with eating disorders was significantly younger than the other groups, childhood prevalence (before the age of 16) was also calculated. The results were analyzed with the chi-square test.

RESULTS

Table 1 shows the point, lifetime, and childhood prevalences of respiratory diseases in each group. Lifetime prevalences were significantly different among the three groups ($p < 0.005$); this was obviously because of the higher value in the group with panic disorder. It is likely that these findings were related to a higher childhood prevalence of respiratory diseases in the group with panic disorder ($p < 0.01$). No differences were found among the three groups with respect to point prevalences ($\chi^2 = 0.856$, $df = 2$, n.s.).

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TABLE 1. Prevalences of Respiratory Diseases in Patients With Panic Disorder, Obsessive-Compulsive Disorder, and Eating Disorders

Prevalence	Panic Disorder (N=30)		Obsessive-Compulsive Disorder (N=30)		Eating Disorders (N=30)	
	N	%	N	%	N	%
Point	3	10	2	7	2	7
Lifetime ^{a,b}	14	47	4	13	4	13
Childhood ^c	12	40	4	13	3	10

^aSeven patients with panic disorder, three with obsessive-compulsive disorder, and one with eating disorder had a history of asthma.

^bSignificant difference among groups ($\chi^2=12.03$, $df=2$, $p<0.005$).

^cSignificant difference among groups ($\chi^2=9.74$, $df=2$, $p<0.001$).

DISCUSSION

In the present study patients with panic disorder, obsessive-compulsive disorder, and eating disorders showed no differences in point prevalence of respiratory disorders. The frequency found of 7%–10% seems to correspond to that found in the general adult population (aged 40–70 years) for chronic bronchitis (17% in men and 7% in women) and wheezing occurring at least once a week (9% in men and 3% in women) (5). Comparison with the study by Littlejohns and associates (5) should be viewed with some caution, since different methods and older subjects were used. Nevertheless, it seems reasonable to conclude that point prevalences are not markedly higher in panic disorder, obsessive-compulsive disorder, or eating disorders.

In contrast with point prevalence, lifetime prevalence was impressively higher in patients with panic disorder than in patients with either obsessive-compulsive disorder or eating disorders. Childhood prevalences were compared because of the approximately 10-year age difference between the group with eating disorders and the other two groups; similar results were obtained.

These results are quite noteworthy. The development of panic disorder would seem to be associated with a history of respiratory illnesses in childhood, disorders that share many of the symptoms found in panic disorder.

It could be speculated that the disturbed respiratory physiology in chronic obstructive pulmonary disease plays a role in the pathogenesis of panic disorder. Severe cases of asthma can induce hypercapnia (3), while in adult patients with panic disorder exogenous CO₂ administration provokes a marked increase in anxiety (6). There is strong evidence in favor of a genetic predisposition to developing panic disorder (7). This predisposition might consist of a hypersensitivity of some CNS structures, such as the locus ceruleus, to CO₂ loading, inducing heightened anxiety. Taken together, it could be hypothesized that repetitive or chronic hypercapnia during obstructive pulmonary diseases in childhood might induce physiological changes in respiratory control or bad breathing habits. The resulting

CO₂ fluctuations would then facilitate the development of panic disorder in subjects who are already genetically vulnerable to this disease.

Alternatively, it could be speculated that disorders affecting the respiratory system predispose one to develop panic disorder merely by means of a learning effect. People who suffered from respiratory diseases in childhood often had accompanying fearful physical experiences during acute episodes of their illness. Later, when a slight arousal occurs, accompanied by symptoms resembling those of their earlier frightening periods, they may become anxious. It is possible that this conditioning effect is not limited to respiratory diseases alone but perhaps also concerns other physical problems, such as minor vestibular or cardiac problems. This hypothesis is supported by the finding that the frequency of vestibular disorders appears to be higher in patients with panic disorder (8; unpublished report of Griez et al.), while mitralis prolapse is also often diagnosed in patients with panic disorder (9). Although the latter studies do not establish the exact causal relationship, it could be speculated that development of panic disorder can be facilitated by various somatic disorders, possibly by means of conditioning mechanisms.

The present study has its limitations: the number of subjects is small and data were obtained by means of a retrospective file study. Furthermore, it could be argued that subjects with panic disorder reported a higher frequency of respiratory diseases because of the hypochondriacal tendencies in patients with panic disorder; yet the same should then hold true for other symptoms. Additional research on the history of diseases in general in patients with panic disorder and, for instance, other anxiety disorders seems therefore necessary. Furthermore, it would be of interest to investigate whether the panic symptom profile of patients with panic disorder and a history of respiratory diseases shows a predominance of respiratory symptoms. These matters are presently being addressed in additional studies in our laboratories. Until these questions have been resolved, the conclusions of the present study are of a preliminary nature.

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Inverse Relationship Between CSF TRH Concentrations and the TSH Response to TRH in Abstinent Alcohol-Dependent Patients

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The authors performed the thyrotropin-releasing hormone (TRH) stimulation test and measured CSF concentrations of TRH in 13 abstinent alcohol-dependent subjects. They found an inverse correlation between the thyrotropin (TSH) response to TRH and endogenous CSF TRH concentrations. This finding supports the hypothesis that as the concentration of CSF TRH increases, anterior pituitary TRH receptor density decreases, resulting in a blunted TSH response to TRH stimulation.

(Am J Psychiatry 1991; 148:1586-1588)

One of the most widely documented biological alterations in psychiatry is the blunted thyroid-stimulating hormone (thyrotropin) (TSH) response to exogenously administered thyrotropin-releasing hormone (TRH). This abnormality in neuroendocrine functioning has been observed in approximately 25% of patients with major depression (1, 2), as well as in such disorders as alcohol dependence (3), eating disorders, and schizophrenia. The etiology of this defect has not been clearly delineated, but a defect in the central regulation of the hypothalamic-pituitary-thyroid (HPT) axis has been posited (4, 5). Increased secretion of hypothalamic TRH into the hypothalamohypophyseal portal system, for example, may produce down-regulation of anterior pituitary TRH receptors, resulting in an attenuated pituitary responsiveness to stimulation by exogenous TRH (2).

The hypothalamus also secretes TRH into the CSF. Concentrations of CSF TRH, therefore, partially reflect hypothalamic TRH secretion. Using a highly specific TRH antiserum, Banki et al. (6) reported higher CSF TRH concentrations in drug-free depressed patients than in control subjects. These observations corroborated an earlier report by Kirkegaard et al. (7). Although these findings support the presence of TRH hypersecretion in depression, the expected inverse

correlation between higher CSF TRH levels and a blunted TSH response to TRH (200 µg) was not observed. To further evaluate the relationship between HPT axis activity and CNS availability of TRH, we performed the TRH stimulation test and collected CSF for TRH measurement in a group of 13 abstinent alcohol-dependent patients.

METHOD

The alcohol-dependent subjects were 13 men hospitalized on a research ward. Their mean±SD age was 51.2±12.2 years. They fulfilled Research Diagnostic Criteria for alcoholism and *DSM-III-R* criteria for alcohol dependence. The *DSM-III-R* diagnosis was based on the Schedule for Affective Disorders and Schizophrenia—Lifetime Version and clinical interviews. All subjects were free of other active axis I or medical disorders, including affective disorders, and their results on urine drug screens were negative at the time of admission. They had been abstinent for at least 3 weeks at the time of testing and were hospitalized under close supervision during this period. Informed consent was obtained.

The comparison subjects were 22 healthy men who were hospitalized at least 1 night before each study. The mean age of the nine comparison subjects given the TRH stimulation test was 44.1±24.0 years, and the mean age for the 13 comparison subjects given the lumbar puncture was 29.1±9.1 years.

The 13 alcohol-dependent men underwent both a TRH stimulation test and a lumbar puncture. The two tests were no fewer than 3 and no more than 15 days apart (6.6±4.2 days). Eight TRH stimulation tests were done before the lumbar puncture, five after.

Presented at the International Society of Psychoneuroendocrinology, Buffalo, N.Y., August 1990. Received Nov. 6, 1990; revision received April 15, 1991; accepted May 10, 1991. From the Laboratory of Clinical Studies, Division of Intramural Clinical and Biological Research, National Institute on Alcohol Abuse and Alcoholism, Bethesda, Md., and the Departments of Psychiatry and Pharmacology, Duke University Medical Center, Durham, N.C. Address reprint requests to Dr. Adinoff, VA Medical Center (116A), 109 Bee St., Charleston, SC 29403.

For both groups of subjects, TRH (500 μ g) was infused at 9:00 a.m. and blood samples were obtained for measurement of TSH and free T_3 at -15, 0, 15, 30, 60, 90, and 120 minutes. Free T_4 measures were obtained at one baseline point. Plasma TSH, free T_4 , and free T_3 concentrations were determined by radioimmunoassays at Hazelton Laboratories. Plasma TSH and T_3 concentrations were defined as mean baseline (the value at -15 minutes plus the value at 0 minutes divided by 2), peak (highest value at 30 minutes or 60 minutes for TSH and highest value at 90 minutes for T_3), maximum change (peak minus baseline) (Δ_{\max}), and total net integrated response (area under the curve minus baseline). Lumbar punctures were performed at 9:00 a.m. following at least a 2-hour bed rest. The first 12 ml of CSF obtained were mixed, aliquoted, and frozen; two 1-ml aliquots were subsequently pooled and assayed in duplicate for TRH concentrations by a specific and sensitive radioimmunoassay (6).

Correlations between measures of TSH response to TRH and CSF TRH were examined with Pearson's r coefficient. Student's t test was used to compare diagnostic groups.

RESULTS

The relationships between the pituitary TSH response to TRH and CSF TRH concentrations were examined in the alcohol-dependent subjects. There was no significant correlation between baseline plasma TSH concentrations and CSF concentrations of TRH ($r=0.22$, $df=12$). There was a statistically significant negative correlation between the net integrated TSH response to TRH administration and CSF TRH concentrations ($r=-0.57$, $df=12$, $p<0.05$). There was also a high negative correlation between CSF TRH concentrations and peak TSH responses ($r=-0.51$, $df=12$, $p<0.1$) and Δ_{\max} TSH responses ($r=-0.52$, $df=12$, $p<0.1$). As expected, peak, Δ_{\max} , and net integrated measures of TSH response to TRH were all significantly correlated ($r=0.98$, $df=12$, $p<0.0001$ for all three comparisons).

Two of the 13 patients had a markedly blunted TSH response to TRH ($\Delta_{\max}<5$ μ U/ml). These two patients also had two of the three highest CSF TRH concentrations.

There was a trend toward significance in the relationship of baseline free T_4 with CSF TRH concentrations ($r=-0.47$, $df=12$, $p<0.1$). No significant correlations between CSF TRH concentrations and baseline free T_3 ($r=0.001$, $df=12$) or peak ($r=-0.14$, $df=12$), Δ_{\max} ($r=-0.18$, $df=12$), or net integrated ($r=-0.25$, $df=12$) responses of T_3 to TRH were observed.

Baseline free T_3 , free T_4 , and TSH concentrations as well as TRH-stimulated TSH and free T_3 responses in the alcohol-dependent subjects were not significantly different from those of the comparison subjects. Two subjects from each diagnostic group had a TSH response to TRH less than 5 μ U/ml. The comparison

group, however, demonstrated a significant negative relationship between baseline free T_3 and Δ_{\max} T_3 response ($r=-0.84$, $df=8$, $p<0.005$) that was absent in the alcohol-dependent group ($r=0.13$, $df=12$). CSF TRH concentrations of subjects with alcohol dependence were not significantly different from those of the comparison subjects.

DISCUSSION

A significant inverse correlation between the TSH response to TRH and the CSF concentration of TRH was observed in 13 patients with alcohol dependence. This finding has both clinical and biological significance. Clinically, CSF measures of TRH may provide a useful measure of HPT axis functioning. In addition, this observation supports the hypothesis that pituitary TSH secretion can be down-regulated by hypothalamic TRH hypersecretion.

There are at least three possible explanations as to why this relationship was not previously observed in patients with depression. First, patients with affective disorders may exhibit dysregulation of their central and peripheral HPT circuitry, resulting in altered relationships among the hypothalamus, pituitary, and thyroid. Second, our alcohol-dependent subjects demonstrated an altered relationship between baseline free T_3 and T_3 response to TRH stimulation. This may indicate the absence of appropriate feedback restraint by T_3 on HPT activity. TRH, unrestrained by T_3 inhibition, may thereby inordinately influence TSH secretion. This would increase the relative contribution of TRH in determining pituitary TSH secretion, accentuating the relationship between TRH and TSH in this group of patients. Third, alcohol-dependent patients as a group may exhibit stable "trait-like" TSH responses to TRH (5), compared with the more state-dependent TSH responsiveness observed in depressed patients. Thus, the timing of the lumbar punctures in relationship to the TRH infusions may be less important in alcohol-dependent than in depressed patients.

Several cautionary notes are required. We assume that CSF levels of TRH are relatively stable over time. TRH may, in fact, be secreted into the CSF in a pulsatile manner, which would limit the importance of single measures of concentration. However, we are unaware of data that suggest this pattern of secretion. Second, correlations do not establish causation and must be interpreted with caution. Finally, the number of patients in this study was relatively small. These findings warrant further investigation in a larger number of subjects and in different patient groups with normal and altered HPT axis function.

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New Policy for References

Effective with the September 1991 issue, *The American Journal of Psychiatry* instituted a policy of listing the names of all authors of work cited in references. Authors of submitted manuscripts and letters to the Editor must include the surnames and initials of all authors in references. The use of "et al." is no longer acceptable.

Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

ALCOHOLISM

The Drunken Society: Alcohol Abuse and Alcoholism in the Soviet Union. A Comparative Study, by Boris M. Segal. New York, Hippocrene Books, 1990, 606 pp., \$40.00.

Boris Segal is the world's heavyweight champion on the subject of drinking in the Soviet Union. The title was not won easily.

Segal was born in Tashkent in 1926, the son of physicians. Both parents were silenced as "enemies of the people." Segal became a psychiatrist, specializing in alcoholism, and came close to being silenced himself. In the 1960s in the U.S.S.R., alcoholism was not a popular subject to specialize in. He wrote books, which were banned. He just escaped arrest when Stalin died.

Frustrated, Segal came to the United States in 1973 and found a home at Harvard. He still had trouble getting published. *Détente* was in vogue, and nobody wanted to offend the Russians. Publishers said he was not objective, and they probably had a point.

Finally, after a herculean effort spanning nearly four decades, Segal produced a major work on drinking in pre-Revolutionary Russia (1) (reviewed in the *Journal* in 1988 [2]). He has now written an equally important book on drinking after the Revolution.

A consummate scholar, Segal has read everything on the subject and talked to everyone willing to talk. In this book, when not writing about alcohol, he provides informed opinions on the history and culture of his native land. He provides a lot of statistics and is the first to admit that they may not be entirely reliable. The fact that he can produce statistics at all about drinking in Russia is something of a miracle. Unless his statistics are fantastically wrong, which seems unlikely, there has been an enormous increase in the consumption of alcohol in Russia since the Revolution.

According to Segal, the Soviets consumed seven times more alcohol in the 1980s than their ancestors did before the Revolution. They drank two or three times more than people in the United States and spent five times more money for alcohol. Mortality from acute alcohol intoxication in the Soviet Union was 278 times higher than the rate in the United States, an astonishing figure. The rate of alcohol-related cases of wife beating in the Soviet Union was 10 times higher than the rate in the United States.

In short, according to Segal, "The scale of national catastrophe due to Soviet escape into self-destructive drunkenness cannot be . . . [equaled] by any other country." You can question the statistics but not the fact that the Russians have a tremendous alcohol problem that seems to be getting worse. Segal compares drinking practices and problems in the United States and the U.S.S.R., broken down by marriage, suicide, the economy, crime, and other personal and social measures.

Toward the end Segal talks about *why* Russians drink so much. (As every schoolboy knows by now, Russia is one of 15 republics, but it is the largest, and when Segal speaks of Russia, meaning the U.S.S.R., it is something the rest of us do; he pays ample attention to differences among the republics.)

In writing about why Russians drink rather than how much, where, and what, Segal falters. He blames poverty, geographical isolation, child-rearing practices, culture, lack of experience in moderate drinking, and, strangely, the "lingering effects of the experience of frequent and heavy intoxication on heredity." (Strange because this sounds suspiciously like Lamarckian genetics, which prevailed in Russia longer than in any other country but presumably is now dead. Undoubtedly Segal realizes this, and the sentence simply came out on the printed page differently than he had intended.)

Segal quotes another authority on Russia, Abram Siniavsky, as saying that Russians drink not from poverty or sorrow but from an "internal inclination toward miracles and the unusual." When the Russian drinks, he says, he is "mystically striving to lead his soul out from earthly equilibrium and return it to its blessed incorporeal condition." One thinks of the great Russian novels and this rings a bell.

Segal concludes by talking about Gorbachev's ill-fated temperance drive. One thousand years ago, a Russian prince said alcohol was the joy of Russia. Just before Christmas last year, the Police Chief of Moscow advocated the legalization of moonshine to protect civil order. He said that the situation might become explosive if the stores did not get more vodka before the holidays. The Muscovites, however, survived the holiday, one reason being their ingenuity. Normally it takes 7 days for mash to ferment. They found they could shorten the process to 4 hours by using the washing machine spin cycle.

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Broadening the Base of Treatment for Alcohol Problems: Report of a Study by a Committee of the Institute of Medicine Division of Mental Health and Behavioral Medicine. Washington, D.C., National Academy Press, 1990, 609 pp., \$45.00.

Any text that is well written, thoughtful, and well researched must be worth reading. These attributes all describe the present report. On the other hand, the relevance that such a detailed text might have for any reader depends on the reader's biases, philosophical bent, and present needs. In the final analysis, this book is worth a brief review by almost anyone interested in the recognition and treatment of alcohol and other substance problems, but clinicians, researchers, and administrators with specific needs will find that individual chapters are worth more intense study.

The text is the result of a committee put together in 1987 by the Institute of Medicine of the National Academy of Sciences. Members of the committee and subsequent working groups were asked to 1) critically review available research and experiences with mainstream and alternative approaches to treatment, 2) evaluate available data on the costs and effectiveness of interventions, 3) review the state of financing for treatment in these areas, and 4) make relevant recommendations for policy and research. The committee was composed of individuals with a variety of backgrounds, many of whom with interests that might be called social psychology.

The committee used the data reviewed to form a vision of a broad array of evaluation procedures and interventions for individuals with a diverse span of alcohol-related life experiences. The vision of "what *could* be" forms the basis for the initial chapter and some of the conclusions presented in the final pages of the report. Other chapters focus on a series of questions felt to be fundamental for the overall task, review existing and potential aspects of treatment, speculate about the applications of these approaches to groups with special needs defined several ways, and gather relevant data regarding the present status of funding in the substance use treatment field.

The overviews and conclusions present a well-reasoned approach that emphasizes a continuum of alcohol-related problems; the need to explore the appropriateness of treatment delivered by psychologists, social workers, and recovering counselors (as opposed to physicians); and the importance of relying as much as possible on community resources for accurate screening and appropriate assignment to treatment. Much thought is devoted to the theoretical need to match the specific intervention to the individual patient's needs and the benefits of creating a feedback mechanism where ongoing evaluations carried out by a federally funded panel of researchers can regularly have an impact on allocation of resources and treatment assignment in an evolving network of intervention techniques.

Although the vision must be admired for its overall scope, it is important to interpret this report in the light of the backgrounds of the people who were appointed to the committee. A parallel document produced by APA or one developed by behavioral psychologists might have presented an entirely different vision. Thus, it is not possible to pronounce this specific approach as "the one" to be followed in the future, but it is appropriate to appreciate the clarity with which the specific point of view is presented. Regardless of theoretical biases, the individual chapters discussing current funding issues will be important reading for many administrators and health care planners, the data in the text and the relevant appendix on evaluations of treatment outcome will be important for both researchers and clinicians with interests in this area, and the balanced discussion of the needs of special groups is important for all clinicians who encounter patients with unique backgrounds and potentially special needs.

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Recent Developments in Alcoholism, vol. 8: Combined Alcohol and Other Drug Dependence, edited by Marc Galanter. New York, Plenum, 1990, 327 pp., \$69.50.

This book is a fine addition to an already comprehensive and distinguished series. Most of the papers in this volume have great relevance to clinicians in the field of substance de-

pendence. The first section is not at all clinical. Although the work presented is very thorough, clinicians might be dissuaded from reading the rest of the book. It is the placement of this section rather than its content that is of concern.

The rest of the volume certainly outlines the changes that are emerging in the field of substance abuse and substance dependence. The contributing authors outline the clinical and basic research variables that contribute to the multiple dependencies affecting chemically dependent populations. The authors begin to look at the variables shared by alcohol, sedatives, stimulants, and tobacco. They search for commonalities in biological factors and receptor modalities as well as in social and environmental factors.

One of the major underlying themes is that this entire field is rapidly expanding and that much of the expansion is empirical and not grounded in a great deal of basic research.

The final sections integrate the present state of knowledge into "state-of-the-art" treatment programs. These treatment programs clearly focus on abstinence from all addictive substances as well as on social and environmental factors that cued the patient into his or her previous pattern of substance use.

This volume and its contributing research should be seen as almost mandatory reading for the many clinicians who work in the substance dependence field.

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AFFECTIVE DISORDERS

Melancholia and Depression: From Hippocratic Times to Modern Times (1986), by Stanley W. Jackson, M.D. New Haven, Conn., Yale University Press, 1990, 431 pp., \$40.00; \$16.95 (paper).

Three basic explorations have guided Professor Jackson in this fascinating journey through two and a half millennia of medical writings on the most human of the medical conditions. The first was an examination of the clinical description of depression in order to assess its consistency and coherence throughout time. The second was a survey of the theories on etiology and pathogenesis, which could be considered a true history of psychiatric ideas and the vicissitudes of medical knowledge. The third and final was a review of the treatment modalities for melancholia and depression, the most technical of our professional tasks. These explorations became the goals of his lifelong scholarly enterprise, and the result, *Melancholia and Depression*, is a captivating intellectual adventure.

In a 23-page introduction the author clarifies terminological and conceptual issues and reviews the essentials of the humoral theory of melancholia, the six "non-naturals" (acquired environmental factors) frequently used in medieval times to explain the variations of similar clinical conditions, and the Platonic and Aristotelian notions of passions, affections, and emotions. He then embarks on eight chapters (section two) that trace the variations in what is otherwise a "remarkably consistent" description of melancholia and depression. This is, without a question, the chronicler at his best, deftly summarizing the different historical periods, the main clinical events, and the intellectual struggles of its protagonists.

Melancholia in ancient Greece and Rome fit the Hippocratic dictum that established it, and every other mental disorder, as a psychological reflection of physiological distur-

bances (*dyscrasias*). Professor Jackson leads us to a renewed respect for Rufus of Ephesus, a teacher of Ishaq Ibn Imran, who, in turn, was the direct source of Constantinus Africanus' *De Melancholia*. Rufus, in fact, made a thorough list of all physical conditions leading to depression and established the basis of a truly preventive program. In all this he is comparable to Galen, the humoralist par excellence and originator of the tripartite classification of melancholia as a primary disease of the brain, as an affection of the blood, and as a hypochondriacal (abdominal) disturbance. This classification, with minor variations, enjoyed several centuries of almost universal acceptance in the Western world.

In medieval times, men such as Alexander of Tralles made remarkable contributions addressing the complexities of the melancholic condition. Arabic medicine set foot on the European intellectual soil through the translations of Gerard of Cremona and his students in Toledo and through the work of Ishaq and Avicenna. To be sure, Constantinus' gigantic review of melancholia set the stage for the main conceptions on the condition well into the early Renaissance. However, medieval times could not be such without the influence of Christianity. Jackson describes the vicissitudes of the concept of acedia, the sin of sloth, its relationship to sorrow and melancholia, and the heavy implications of the need for confession as a form of healing. It may be that the use of opposites, antinomies, or even dichotomies started with the flowering of scholasticism and the works of its main proponents such as Thomas Aquinas, Cassian, and David of Augsburg. When acedia acquired a connection with the passions, it also began to be described in physiological terms with a timid acceptance of the "imbalance of the humors," a medical frame of reference that implied, in later medieval times, a lesser degree of and reduced responsibility for sinfulness, thus allowing the sufferer to be less harshly judged.

The author starts the chapter on melancholia in the Renaissance by saying that the transition from the Middle Ages did not bring any substantial change in how melancholia was described, explained, or treated. However, Paracelsus' contribution—the inclination to disregard the supernatural causes espoused by the scholasticists—may have been as decisive as his rejection of humoral theory, which Jackson calls "the beginning of a trend that would greatly affect explanations of melancholia in the following century." The same can be said of Bright's use of metaphors, or of Platter and his portentous advocacy of the most narrow diagnostic criteria. During the same period, Burton's *The Anatomy of Melancholy* became the most comprehensive survey on the subject, hailed even now as an inspiring encyclopedic forerunner of notions such as premorbid personality, melancholia and creativity, and useful classificatory schemes.

The last four chapters of this section deal with the concept, classification, and treatment of melancholia in the last four centuries. Forced to cite only one author per century, as an arbitrary summarization of the contributions made then, I would choose the following. In the seventeenth century, Thomas Willis laid the foundations of chemical explanations of melancholia. Cullen's neural explanations during the eighteenth century were a dazzling announcement of present-day neurotransmission, marking the peak of the mechanistic explanations of depression such as the slowing of the patient's circulation associated with a slow and dejected state, or the excited (electrically charged) state explaining the extravagances of the manic patient. Griesinger, in the nineteenth century, favored the unitary disease concept, but his greatest contributions were the descriptive separation of melancholia from hypochondriasis and his devotion to the credo of "brain psy-

chiatry" and to the biological basis of all psychiatric conditions, specifically depression. Finally, in the twentieth century, Kraepelin overshadows others with his classical separation of the major psychoses, the consecration of the dichotomies, and the categorical approach to diagnosis. Jackson's chapter on the twentieth century includes excellent summaries of the different classificatory systems predominant in the contemporary scene, the contributions of Freud and other psychoanalysts, and recent biological, psychological, and sociocultural themes and treatment trends.

In section three Jackson studies the connections between mania and melancholia; hypochondriasis and melancholia; grief, mourning, and melancholia; and religion, the supernatural, and melancholia. Section four addresses melancholic variants such as lycanthropy (curiously, Nebuchadnezzar, a *case princeps*, is not mentioned here), love melancholy, and nostalgia. In essence, this is a recapitulation of different concepts with an emphasis on the emergence of biopsychosocial approaches, distinctions of clinical and nonclinical states, and the short life of some notions such as religious melancholia, erotomania as a melancholic condition, and nostalgia. The last chapter is appropriately titled "Overview and Afterthoughts." The parade of theories and the plethora of metaphors are reviewed again. The diagnostic confusions and the efforts at localizing specific lesions, the impact of external events, and symptoms as forms of communication are examined against the background of effective therapeutic approaches and the frustrations of chronic, treatment-resistant cases.

With works of this magnitude one shies away from trying to point out errors of commission or omission. Of course we are amazed at how much more we know now and yet how similar some of our basic conceptions and even management approaches are to those advocated many centuries ago. Did the Stoics not set the notion of multiaxiality? Did Soranus and many others, centuries later, not struggle with the distinctions among depression, obsessive-compulsive disorder, schizophrenia, and hypochondriasis? Was Paracelsus not using the same medicines for different conditions, very much as we do today (1)? Are Du Laurens' descriptions in the Renaissance not as faithful as modern descriptions of psychotic depression? Were the corpuscular dynamics and hydraulics and electrical experimentation of the eighteenth century not setting the stage for later biochemical speculations and findings as well as neurophysiological correlates? Can Cullen not be called a pre-Kraepelinian, and is Rogers' case not one of substantial comorbidity? And what about Esquirol's outlining the crucial significance of external events more than 200 years ago, and von Feuchtersleben's speculating about membrane permeability, or Maudsley's objecting in the 1920s to the symptomatic separation of the two major psychoses, as Pope and Lipinsky (2) did in the 1980s? Of course, Freud in his infinite wisdom may have foreseen the close relationship between what we now call borderline personality disorder and depressive variations such as dysthymia (3). And on and on.

There are repetitions in this book, to be sure. There are also some omissions due to the fact that it was published in 1986, before *DSM-III-R*, for instance. Some of the most recent modifications of the learned helplessness theory (4) are not included. It would have been good to recognize works and contributions from other than European authors, such as those of Latin American and Third World investigators (5). Although patients' self-reports are included, the social, cultural, and historical facets of depression and melancholia could have been examined as well through the contributions of the *literati* of each period. Dickens, Shakespeare, Moliere,

Kafka, Cervantes, and Garcia Marquez have made illuminating contributions to the description and the actual experience of the illness, but that may be the topic of another book by Jackson or by other authors with a similar breadth of knowledge and scholarly devotion.

Sauri (6), an Argentinian epistemologist, said that there are two ways to approach the study of history: one developed by the chroniclers and the other practiced by the philosophers. In a way, Jackson has trod masterfully between these two pathways, perhaps with a bit more skill in the former, but with wonderful insights coming from the latter. One cannot expect a Kuhnian interpretation of events without first knowing a Herodotian account of what happened then and there.

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Depression: An Integrative Approach, edited by Katia R. Herbst, M.A., Ph.D., and Eugene S. Paykel, M.A., M.D. New York, Heinemann Medical Books in association with the Mental Health Foundation (Stoneham, Mass., Butterworths, distributor), 1989, 249 pp., \$75.00.

As promised in the title, this book presents a wide-ranging overview of current thought on depression. It invites the reader to compare and integrate psychological, biological, and sociological perspectives on the disorder. Based on the proceedings of a 1988 London conference, with additional chapters commissioned to provide a broader scope, a group of established British investigators and clinicians review topics pertaining to the etiology and treatment of depression. The book highlights what we know and what we do not know about "biopsychosocial" approaches to depression.

The stage is set in Professor Paykel's introductory overview on classification and epidemiology of depression, with a pragmatic comparison of nosological approaches taken by *DSM-III-R* and *ICD-10*. The second section of the book surveys factors contributing to the onset of depression. Chapters by George Brown and by Paul Bebbington and Peter McGuffin examine the role of life events, social support, and personality variables in the onset of depression. Biological points of view are represented in a brief review of molecular genetic approaches to manic-depressive illness by Hugh Gurling and a synopsis of neuroendocrine challenge studies in depression by Stuart Checkley. J. Guy Edwards contributes a comprehensive review of the (limited) evidence for depression in response to a range of medications (e.g., antihypertensive drugs, oral contraceptives, and neuroleptics).

The third section, The Life Cycle and Depression, provides

clinically sensitive reviews of unique characteristics of depressive syndromes occurring in adolescence, in the puerperium, and in later life. Distinctive biological, social, and psychological factors are highlighted. For the psychotherapist with limited experience with patients in these specialized settings of the life cycle, there is much valuable clinical wisdom here.

The final section of the book outlines selected aspects of the management of depressive disorders. There is a practical introduction to cognitive therapy of depression by J. Mark Williams, with a review of outcome studies. The chapter on antidepressant medications by Stuart Montgomery provides interesting perspectives on the issue of anxiety in depression, the role of selective serotonin uptake inhibitors, and long-term treatment with antidepressants. The chapter by Keith Hawton on assessment and management of suicide attempts includes a very practical review of predictors of future suicidal behaviors. The last two chapters consider the experience of the depressed patient in two nonpsychiatric settings—the general practitioner's office and self-help groups.

This book is clearly not intended to be encyclopedic and does not cover the range of traditional textbook topics such as psychiatric comorbidity, comparison of psychotherapies, psychodynamic perspectives, inpatient treatment, or pharmacological approaches to treatment-resistant depression. The reader also needs to be prepared to switch between chapters developed as literature reviews and those more selectively focused on the individual author's own research interests. The book has been carefully edited for stylistic consistency across chapters, however, and all contributions are highly readable. For the experienced clinician as well as advanced trainees, this volume is a valuable complement to the more comprehensive texts. Each author is alert to the importance of other points of view, and I finished the book feeling optimistic about future directions in integrating psychosocial and psychobiological perspectives on depression.

DAVID C. JIMERSON, M.D.
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Depressive Disorders and Immunity, edited by Andrew H. Miller. Washington, D.C., American Psychiatric Press, 1989, 187 pp., \$20.95.

This book gives the reader a basic education in immunity as it relates to psychiatry and mental illness. It consists of eight chapters; the editor is coauthor of four. The first two chapters give the reader a basic orientation to this area, which most of us badly need. We are introduced to immunobiological concepts and are told about the organization of the immune system and its various cellular components and lymphocyte activation, as well as the structure, organization, and function of surface molecules in the immune responses. In the chapter "Neural-Immune Interactions" we are told that numerous investigators have demonstrated an association between psychological stressors and immune function. Neural lesions are connected with changes in cellular immunity, and localized lesions in particular areas of the brain are associated with changes in the immune system. Lesions of the anterior hypothalamus are connected with fewer deaths due to anaphylactic shock than are sham and control lesions. Apparently, catecholamines have a stimulatory effect on the immune system at low concentrations and an inhibitory effect at high concentrations. The fascinating work of Ader and Cohen in the behavioral conditioning of immunity is summarized. However, I was struck by the sobering statement that "nevertheless, the

relationship between stress and the decrease in the various immune parameters is exceedingly complicated. In no instance is there any evidence that the alterations in immune function are clinically relevant. No study has clearly demonstrated an increased incidence of morbidity or mortality associated with the immunological changes that have accompanied these stressors."

The remaining chapters are devoted to the issue of changes in the immune system as seen in major depressive disorders. There is a real question concerning whether the immune changes seen in major depression are specific for this disorder. The observation that depression is associated with altered immunity, we are told, suggests that this process may influence the onset and course of mental disorders. A chapter is devoted to the effects of tricyclic antidepressants and immunity. The tricyclics seem to have a direct inhibitory immunological effect. However, since these drugs alleviate depression, they may indirectly reverse any mood-associated alterations in immune function.

In a chapter on immune function and glucocorticoid receptor regulation we are told, "Several components of the immune system produce biologically active peptides that are capable of activating the neuroendocrine axis as well as influencing other cells in the immune system." The relationship between β -adrenergic receptor and immune function in normal and depressed subjects is not fully understood, but there is optimism that the interrelationship among β -receptors, immune function, and depression will be known in the not-too-distant future. In the final chapter the authors speculate on a connection between antibodies to Epstein-Barr virus and its relationship to major depression. This is a highly speculative area. The connection between the two is not established.

This interesting book gives the reader an excellent overview of the current status of knowledge about immune mechanisms and their association with psychological illness, especially depression. This is an exciting, new area that holds great promise, but at this point its clinical relevance has yet to be shown.

NORMAN B. LEVY, M.D.
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Combined Pharmacotherapy and Psychotherapy for Depression, edited by Donna W. Manning, M.D., and Allen J. Frances, M.D. Washington, D.C., American Psychiatric Press, 1990, 181 pp., \$25.00.

This book is a concise and worthwhile review and presentation of findings. It serves as an overview of material that has provoked vigorous debate as well as a reminder that treatment modalities can be adapted to a patient's individual needs. This addition to the Progress in Psychiatry series, edited by David Spiegel, M.D., has several fundamental strengths that are readily apparent. This volume is succinct, economical, and well referenced, and the contributors are well respected. The organization is particularly attractive in that it progresses from a review of the literature through the various treatment modalities culminating in some basic and helpful clinical vignettes. The issues of combination therapy in the treatment of depression have not only generated a considerable body of research but also been the fulcrum for a breach between the "pharmacologist" and "therapist." It is commendable that this book's editors and contributors make a concerted effort not to foster any widening of this lapse in continuity. This perspective is clearly stated by Drs. Weissman and Klerman: "The decision to use medication in the treatment of depression

should be based on the patient's severity of symptoms, quality of depression, duration of disability, and response to previous treatments. It should not be based on the loyalties or training of the professional, as is too often the case in common clinical practice."

Throughout the book, the contributors provide brief reviews of the specific literature for each treatment modality. Most of the data and results are presented in easily digestible tables and graphs. A primary goal of this volume is to furnish the study design in enough detail that comparable investigations may be conducted. The criteria used for inclusion and exclusion, initial evaluation, and treatment response are clearly documented with extensive references. This quality work is combined with numerous correlations with previous and ongoing research.

The majority of the contributors conclude that combined pharmacotherapy and psychotherapy is at least as efficacious in treating depression as either treatment alone. Reasonable evidence is provided that combination therapy provides some prevention of relapse and lowers study attrition. Clearly, a definitive answer to the question of which treatment is superior has not been forthcoming. Still, the need to identify subgroups of depressed patients and tailor individual treatment plans is supported by the contributors.

All too often the basic ideals of treating patients with depression are lost in treating the depression. The final chapter by Drs. Salzman and Bemporad provides information that will be useful to the clinician, particularly anyone in training. An effort is made to identify some of the treatment phases, dynamic issues of the individuals involved, the meanings of medications, and the doctor-patient relationship. Salzman and Bemporad give a metaphor for the initial treatment of depression—"If a house is on fire because of faulty electrical wiring, the first task is to put out the fire, not rewire the house." The clinical vignettes illustrate some problems that are encountered during combination therapy.

The editors impart a final synopsis and combine this with their clinical experience to provide good closure to this volume. *Combined Pharmacotherapy and Psychotherapy for Depression* is a useful addition to the library of anyone who treats patients. It provides up-to-date information on the efficacies of the various treatment modalities, enough detail for the clinical researcher to design comparable studies, and reminders that the treatment of patients is paramount. I would add only, "Don't forget to rewire the house."

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Comorbidity of Mood and Anxiety Disorders, edited by Jack D. Maser and C. Robert Cloninger. Washington, D.C., American Psychiatric Press, 1990, 869 pp., \$59.95.

This is an important and exciting book and covers a topic of current interest. The relationship of multiple psychiatric disorders occurring in the same patient over time provides difficulties relating to classification and treatment. Although the focus of this volume is on anxiety and mood disorders, comorbidity with other conditions and other patient groups is also described. For example, there are chapters relating to somatization, alcohol and substance abuse, dysthymia, obsessive-compulsive disorder, and eating disorders. Additionally, there is a very nice chapter on the comorbidity of anxiety disorders and depression in childhood.

The basis for this book was a conference relating to comor-

bidity, and the 40 chapters are written by individuals knowledgeable about the various areas of interest described. What was amazing to me was how well the chapters flowed one after another, reflecting what must have been an inordinate effort on the part of the editors to provide coherence to this volume. They did a fine job.

The book is divided into eight major sections: Introduction, Classification Issues, Population-Based Studies, Treated Samples and Longitudinal Studies, Family and Genetic Studies, Biologic Studies, Theories of Anxiety and Depression, and Research Issues, Methodology and Assessment. The references go into at least 1988, and the referencing is somewhat unique in that references are not given for each chapter but instead there is a master reference section at the back of the book that includes all references given. This actually decreases the size of this book considerably because a given paper could have been referenced in each of the 40 chapters.

I appreciate having access to this volume. The chapters are of interest and provide up-to-date thinking regarding important issues. The reference list is quite useful. A number of the studies cited in this volume are also critically reviewed. It is difficult to determine how useful this book would be for the clinician or the psychiatric researcher who is not involved in the treatment of anxiety and mood disorders. It is certainly a useful volume for researchers involved in issues relating to comorbidity or issues relating to anxiety or mood disorders. I would recommend it most highly for this target audience.

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The Genetics of Mood Disorders, by Ming T. Tsuang and Stephen V. Faraone. Baltimore, Johns Hopkins University Press, 1990, 176 pp., \$40.00.

This book is like vanilla ice cream: good, but not exotic. To carry the metaphor further, it is served unadorned in a dish without sauce or whipped cream. Nevertheless, it nourishes. Tsuang and Faraone have produced a small, nicely written, reasonably referenced, hardbound monograph summarizing the family, twin, adoption, linkage, and marker literature regarding manic-depressive illness. The chapters are straightforward, well-organized, balanced descriptions of the often-cited studies assessing the familialness of manic-depressive illness. The conclusions are all reasonable. If I had not received a copy to review, I would purchase one as an easy-to-use reference source. I will encourage my department colleagues and our residents to read it. I encourage anyone who wants to know the basics of this literature to read it. To paraphrase David Copperfield's friend, Mr. Macawber, "In short, I liked it." I like vanilla.

Therefore, do not misconstrue what follows. The book is a bit odd in that it has no foreword, no dedication, no indication of why it exists. It induces existential reviewer-anxiety. A reviewer is supposed to place a book in some social or scientific context, and such connection is often found in what the authors tell us about their motivations and efforts in writing their book. Not so here. Writing a book is hard work. Why did Tsuang and Faraone write this one and who do they hope will read it?

This apparent lack of mission sets the tone for all discussion. Although reference is made to potential comorbidity among depressive syndromes, anxiety and mood states, and schizoaffective disorder and manic-depressive illness, there is no speculation about what it all means. Tsuang and Faraone pre-

sent consensus answers. Being scholarly, they suggest that there are disturbing, unanswered questions about the genetics of manic-depressive illness, but their focus is clearly elsewhere. Perhaps this is also true for the field of traditional, clinical psychiatric genetics. Perhaps it is in a stage of consolidation of information and organization of old ideas, as if waiting for Triptic gene maps to show it the way. If true, I think it unfortunate, because even if sociobiologists are correct and we are mere containers for our DNA, short of mapping all DNA and all containers, someone still has to decide which containers to choose in unraveling the DNA of manic-depressive states. Tsuang and Faraone touch on this in their first and last chapters ("Diagnostic and Methodological Issues" and "Summary and Conclusions"), but they do not pursue it. Although I like vanilla, I also like hot fudge, hot peppers, and the apparently hot potatoes of psychiatric genetics. A pleasant dish can sometimes leave one hungry.

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SCHIZOPHRENIA

Understanding Psychotic Speech: Beyond Freud and Chomsky, by Elaine Ostrach Chaika. Springfield, Ill., Charles C Thomas, 1990, 310 pp., \$53.75.

Irregularities of speech have long been considered to be a hallmark of schizophrenia (1). These language alterations make it harder—and at times impossible—for the listener to discern what the speaker has in mind to say. Although the effects on the listener are fairly clear-cut, the nature of these language alterations themselves are much harder to determine. It is certainly the case that the *content* of what the schizophrenic patient is attempting to express is often bizarre and confusing and therefore difficult to understand. However, there is now considerable evidence suggesting that the diminished comprehensibility of schizophrenic speech can also reflect violations of those formal rules and constraints which ordinarily govern language behavior. Elaine Chaika, a linguist, has made a series of important contributions to this area during the last two decades. A synthesis of her work, embedded in a scholarly review of developments in the general field of linguistics over the same time period, has yielded this book, which is worthy of serious attention.

"Formal rules" herald back to a brand of linguistics elaborated by Noam Chomsky and his co-workers and refer to human mental competencies underlying the successful combination of sounds and syllables into words and the successful combination of words into grammatical forms. Chaika provides innumerable examples of schizophrenic utterances that clearly demonstrate violation of linguistic rules, such as the production of gibberish, nonwords, and syntactic errors, that seem *not* to be the result of intentional word play, deviant ideational content, or willful obfuscation of meaning, as others have claimed. Later chapters describe an interesting experimental task she conducted: schizophrenic subjects, manic subjects, and normal subjects were asked to describe a simple story shown on a silent videotape; the responses of the psychiatric patients were extremely deviant compared with those of the normal subjects.

Newer branches of linguistics, generally referred to as pragmatics and discourse analysis (post-Chomsky developments—hence the title's reference) are dealt with at length; these do-

mains of study attempt to characterize factors lying outside sentence structure that confer meaning to utterances. These factors include 1) the social purposes of language, 2) how tacit, shared knowledge is used to organize conversations, 3) how multiple sentences are tied together to create topics within and between speakers, and 4) how words actually "do things" that extend beyond the concrete meaning of the words themselves (e.g., a teacher entering a classroom with the comment, "Someone's a bit noisy" is not just informing the students about decibel levels but indicating the need for someone to quiet down). Chaika demonstrates that schizophrenic subjects consistently fail to be guided by the pragmatic and discursive aspects of conversational behavior. She makes a number of important points.

First, she makes the point that analyses of lexical cohesion, a fairly standard approach to characterizing multi-sentence discourse produced by schizophrenic subjects that is based on an assessment of the degree to which the nouns and pronouns of an utterance explicitly refer to the same things, do not go nearly far enough in capturing what is deviant, at a "extra-sentence" level, in schizophrenic utterances. She also points out that a constraint on conversational behavior is that the speaker says only enough to make a point. Psychotic speakers often say too much and may include material that is not relevant to the conversational topic. Another constraint on conversational behavior is that a speaker describing a series of events should organize the account to reflect the temporal ordering. For example, if event B followed event A, the narrative describing the events should describe event A before event B. The psychotic subjects in the author's study often did not conform to this expectation. She points out that a factor contributing to the paranoia of psychotic patients may be their inability to derive proper implications from higher-order, pragmatic constraints on language behavior.

Although the empirical study described by the author produced many important observations, it also has some limitations. For instance, she lumps together the irregularities of schizophrenic and manic subjects. I believe that this is not warranted at this time; there is evidence that these two groups of patients produce quite distinct types of deviance (2, 3), although the degree of their distinctiveness remains an unanswered empirical question. Second, selection criteria for subjects in Chaika's study are not made fully explicit, but it is implied that they were selected only if they had already shown evidence of certain types of problems. It is therefore not at all surprising that the linguistic performance of the psychiatric patients was much more deviant than that of normal speakers. This research strategy is problematic. One does not learn, for instance, the actual percentage of randomly sampled patients who produced the kind of deviance described by Chaika; other research suggests that abnormal levels of linguistic deviance, not necessarily as severe as that highlighted by Chaika, are discoverable among schizophrenic patients who are randomly selected (4). Statistics reflecting the frequency distribution of different types of deviance within each of the three subject groups would have helped the reader to objectively assess qualitative differences of errors produced by psychotic versus normal subjects (normal speech is fraught with imperfections as well), but these data are not presented; statistical analyses are available only for cohesion data.

I think the book raises some other questions and concerns as well. First, the author argues that there is a relationship between deviant eye-tracking patterns elicited in schizophrenic subjects and deviant speech with derailments and intrusions of irrelevant material (pp. 43, 44). Although these

different types of pathology may in some sense be analogous, the author fails to cite a study by Solomon et al. (5) indicating that, statistically speaking, the association between eye-tracking dysfunction and disordered speech in psychiatric patients is very weak. Readers should therefore not be misled into concluding that there is a common neurocognitive mechanism for eye-tracking and speech difficulties in schizophrenia.

Second, I was surprised that the author did not more fully discuss the possible overlap between schizophrenic deviance and the different types of organic aphasia. Chaika herself was one of the early proponents of the hypothesis that such an overlap exists. Although she does suggest that a certain pattern of deviance is specific to psychiatric patients with psychotic disorders (p. 7), subjects with aphasia certainly can produce gibberish, neologisms, and syntactic errors. The relationship between the disorders of schizophrenia and neurological disorders may be useful in identifying and localizing cortical dysfunction in schizophrenia and can be conceptually linked to other studies suggesting that at least a subgroup of schizophrenic patients suffer from a dominant hemisphere disturbance (6-8).

Third, I am not particularly keen on using the term "psychotic speech." "Psychosis" in psychiatry generally refers to conditions that include hallucinations, delusions, and disorientation, where one's sense of what is objectively real is impaired. Psychosis, then, includes phenomena that roughly fall in the category of judgments and perceptions but decidedly not speech. Empirically, psychosis and irregularities of speech occur quite independent of each other, and many patients demonstrate speech deviance after the psychotic phase of their illness has passed.

The last chapter argues that inferences regarding the deviance of our patients' utterances should be based first on the rules of speech, language, and conversation and should not immediately yield to prefashioned psychoanalytic notions about the nature of schizophrenia (hence the reference to Freud in the title). Although the first part of this statement is well founded and worth making, to criticize psychoanalytic interpretations of linguistic deviance produced by schizophrenic speakers is a bit like beating a dead horse. Good clinicians these days, whether they are psychoanalysts or not, should never dismiss what the schizophrenic patient is struggling to say with superimposed "interpretations"—no matter how garbled the speech—but should fully join with the patient in a collaborative effort to try to make sense of what he or she means.

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Depression in Schizophrenics, edited by Richard Williams and J. Thomas Dalby. New York, Plenum, 1989, 253 pp., \$62.50.

Although depression was identified as an integral part of schizophrenic symptoms by early writers such as Kraepelin and Bleuler, it has lost over the years its significance and emphasis in descriptive formulations of schizophrenia. This was in part caused by the emergence of the "schizoaffective" concept and more recently by the more exclusive emphasis on positive and negative symptoms as sufficient syndromal explanatory concepts. Fortunately, we are witnessing a reemergence of interest in the phenomenon of depression in schizophrenia as an additional psychopathological syndrome as well as interest in its prognostic, morbid, and treatment implications. This renewed interest is due to the increased recognition of possible overlaps of negative symptoms and depression in schizophrenia and to the more sophisticated assessment techniques available. Furthermore, there is more awareness of the lower quality of life of schizophrenic patients due to the many disabling aspects of their condition.

This book has its origin in a 1988 conference, but the results of some of the studies included are still relevant today. The chapters are grouped into four sections: Theoretical Aspects, Phenomenology, Suicide and Prognosis, and Treatment Approaches to Depression in Schizophrenics. Brockington sets the tone in the beginning by arguing elegantly for a model of schizophrenia that represents the sum total of a wide array of distinct yet interrelated morbid processes transcending more traditional discontinuous models with firm nosological boundaries. Genetic data presented by McGuffin et al. also favor a more dimensional approach, although they do not include Crow's reanalysis of genetic data (1). Flor-Henry reviews his work on brain lateralization of psychosis, arguing that right hemispheric disturbance results in depressive symptoms and left hemispheric disturbance leads to schizophrenic symptoms. He also argues for a continuum concept based on findings of overlapping distribution of underlying neuropsychological impairments in affective, schizoaffective, and schizophrenic psychoses.

Samson et al. present a carefully conducted cross-sectional comparison of schizophrenic patients and patients with unipolar depression in the Brockton Veterans Administration-Harvard study. A high degree of concomitant affective disorder was found in the schizophrenic subjects. Negative symptoms were differentiated from depression and were found highest in schizophrenic subjects without affective symptoms and lowest in patients with unipolar depression, which again points to a continuum model of negative symptoms. A very similar point is made by the study of Owens and Johnstone, but on the side of depression. These authors found that rates of depression were highest in patients with affective disorders and lowest in schizophrenic patients without affective symptoms. Their study does not support the concept of neuroleptic-induced akinetic depression. Regarding the tem-

poral relationship of depression and psychotic symptoms, Green et al. found a less frequent onset of depression than expected by chance in the postpsychotic phase, somewhat challenging this time-honored clinical concept.

Attesting to our ability to assess depression independently from negative symptoms, both Pogue-Geile and Williams et al. found no correlation of negative symptoms with depression in stable schizophrenic outpatients. On the other hand, in a group of acutely ill patients, the Addingtons found a high degree of overlap between the two syndromes, pointing to a more phase-specific interaction between the two syndromes.

In the section on suicidal behavior, Roy presents an excellent review on the incidence and the short- and long-term risk factors of suicidal behavior in schizophrenic patients. He points to the difficulty in the long-term prediction of suicidal behavior. This is particularly important in the face of the alarmingly high rate of suicide among young, relatively early-phase patients with schizophrenia described by Westermeyer and Harrow. They list as risk factors male gender, white ethnicity, higher educational level, gradual onset, and paranoid subtype. They point to these patients' high expectations for themselves in the earliest phases of their illness and their subsequent profound dissatisfaction with the quality of their lives.

The treatment chapters do not add much except for the excellent review by Siris of the use of antidepressants in schizophrenia and the now classical study by Van Putten et al. on the neuroleptic dysphoria syndrome, which actually should be called the extrapyramidal dysphoria syndrome. It may be that this syndrome applies primarily to patients treated in the acute phase and with high-potency neuroleptics.

Overall, this book reflects accurately and fairly extensively the state of the art regarding depression in schizophrenia and addresses the major issues of potential unclear boundaries, such as negative symptoms and neuroleptic-induced extrapyramidal side effects. It also addresses important clinical issues such as the prediction of suicidal behavior in these patients. Given the fact that the book contains the original studies on which its conclusions are based, the clinician may find it too detailed and data oriented. However, it constitutes valuable reading for the researcher and the clinician who is particularly interested in the depressed schizophrenic patient.

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JEAN-PIERRE LINDENMAYER, M.D.
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Recent Advances in Schizophrenia, edited by A. Kales, C.N. Stefanis, and J.A. Talbott. New York, Springer-Verlag New York, 1990, 395 pp., \$49.00.

This multiauthored volume initiates the new Springer-Verlag International Perspectives Series: Psychiatry, Psychology and the Neurosciences and forms a written record of the Third Annual Pennsylvania Conference on Schizophrenia, held in Harrisburg in March 1988. The most striking feature of the book is the extremely broad range of topics covered: schizophrenia and its treatment are considered from prehistoric times onward, in Western countries as well as in China and Africa, and from research perspectives ranging from molecular genetics to evaluation of psychosocial treatment. Each chapter provides a review of relevant past work followed by

a substantial foray into the technical details and problems of the subfield addressed, as, for example, in the descriptions of "pulsed field gel electrophoresis" and the colorful "jumping libraries" and "zoo blots" in the chapter on molecular genetics by DeLisi and Lovett. Three chapters deal primarily with history and the concept of schizophrenia, six with biology, three with vulnerability, stress, and psychosocial issues, and six with care delivery systems around the world.

Although the chapters are loosely organized into three sections, Conceptualization of Schizophrenia, Recent Advances in the Diagnosis and Treatment of Schizophrenia, and Delivery Systems for Managing Schizophrenic Patients, there are few attempts to draw any overall conclusions or provide synthesis of the diverse research efforts. Two intriguing chapters are exceptions to this rule, "Modular Disjunction in Schizophrenia: A Framework for a Pathological Psychophysiology" by Cleghorn and Albert and "Meaning of Structural Changes in the Brain in Schizophrenia" by Crow. These chapters advance creative, synthetic hypotheses in the fields of functional and structural brain abnormalities, respectively. Still, some readers may find the viewpoints and literature sources in these chapters somewhat selective.

The historical chapters are thorough, but the material is familiar to most psychiatrists.

Schulsinger and Parnas review the Copenhagen High Risk Study, which assessed 10–20-year-old children of schizophrenic mothers in 1962 and followed them up in 1967, 1972, 1980, and, for the most part, 1988. Behavioral precursors to schizophrenia and schizotypy and early environmental factors associated with later schizophrenia in these genetically vulnerable individuals are presented.

Chapters on molecular genetics by DeLisi and Lovett and on brain imaging by Pahl, Swayze, and Andreasen provide rather attentive introductions to the techniques involved. Indeed, these methods offer more future technological potential than they do in the way of current conclusive results for the field of schizophrenia. The discussion of the controversy over D₂ receptor imaging by positron emission tomography is quite good. (The Baltimore group found more receptors in drug-naïve schizophrenic subjects, but the Stockholm group did not.)

A chapter by Meltzer presents in great detail the largely basic science support for hypotheses explaining the unique actions of clozapine in schizophrenic patients. The unstated implication is that these hypotheses may be tested by continued screening for new compounds. Notable in the chapter on psychopharmacology is Kane's analysis of the issue of the haloperidol "therapeutic window" and neuroleptic blood levels in general. The author makes some highly relevant points and recommendations for future research, despite his neglect of the literature on the active metabolite, reduced haloperidol. Readers seeking a discussion of such adjunctive medications as benzodiazepines and lithium will not find one in this chapter.

The discussion of risk factors and psychosocial treatment evaluation occurs in several chapters (by Goldstein, by Mueser, Liberman, and Glynn, and by Tarrier and Barrowclough) and is, by and large, lucid. The uniform application by all authors of the vulnerability stress model of Zubin and others lends attractive consistency to this enlarging research area. There is an interesting discussion by Goldstein of his own work and that of Tienari et al. addressing the question of whether, among individuals at genetic risk for schizophrenia (defined by family history of the disease), stressful family interactions increase the risk for developing the illness later in adolescence and adulthood. Another result presented is that expressed emotion might be evaluated at several time points

in relation to an episode of relapse, since it may be state dependent rather than enduring.

The verdict on family interventions and social skills training as presented in the chapters by Goldstein and by Mueser et al. continues to be definitively positive. As suggested by Tarrier and Barrowclough's chapter, however, these treatments, like medication, must often be continued to preserve the protection against relapse.

The diversity of the final chapters on care delivery systems around the world is best illustrated by the fact that the authors' reactions range from outrage to pride. Although these chapters deal largely with how different political and cultural systems have or have not managed to meet the varied needs of schizophrenic patients, the further hope is that some practical truths about optimal treatment and its optimal administration may emerge. The common theme of transition to community-based treatment is foremost, but other interesting observations are made. The chapter by Tarrier and Barrowclough reports data suggesting that lower rates of households with high expressed emotion may explain the more benign course of schizophrenia in developing countries. The suggestion to use the same trusted provider throughout treatment of exacerbation and maintenance of remission may seem logical but often goes unheeded.

Reading the book straight through brings out its almanac-like features and is not advisable, except perhaps for the schizophrenologist. Those already following developments in the schizophrenia field must wade through a good bit of background and explanatory material to find the important discussions of new results. More likely, this volume will prove a useful reference for readers in a variety of disciplines, ranging from students and administrators of public policy to researchers and practitioners in the mental health professions. An outstanding aid to reference use is the end-of-chapter summary: each chapter is accurately and religiously recapitulated in its final subsection. Another feature of this text applies to any publication bringing us the "state-of-the-art" in schizophrenia but is a ray of hope to its subjects and readers: it will likely soon be out of date.

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Depression in Schizophrenia, edited by Lynn E. DeLisi, M.D. Washington, D.C., American Psychiatric Press, 1990, 160 pp., \$22.50.

This is an excellent book with contributions by many of the major researchers in this field. The editor should be commended for soliciting chapters from both North American and British workers, giving the book a cosmopolitan flair and a healthy dose of the Queen's English.

A central bias that the book attempts to correct is an oversimplification of the Kraepelinian division of psychoses into the schizophrenic and affective disorders, which assumes that individuals with "real" schizophrenia should not have affective symptoms. This viewpoint ignores the distinction between the prevalence of a symptom and its diagnostic value and assumes that depressive symptoms in schizophrenia need to be explained away. They are seen as evidence for a chimeric disorder, schizoaffective psychoses, or as secondary to medications, negative symptoms, recovery from psychosis, etc. However, as the chapters by Leff and by Hirsh et al. make amply clear, depressive symptoms are part and parcel of schizophrenia. Their progress generally follows that of psychotic symp-

toms, and they cannot be readily explained as secondary to treatment. Does this mean that Kraepelin was wrong? Not at all. Both chapters rely on the same schema to incorporate these findings into our traditional diagnostic system, a hierarchical model developed by Foulds and Bedford. This model arranges psychiatric symptoms in a pyramid, with nonspecific psychological symptoms at the bottom, followed by symptoms of neurotic disorders, symptoms of affective psychoses, symptoms specific to schizophrenia, and symptoms of organic brain disorders. Patients at any level may have symptoms from any level below them. With such a schema one would expect individuals with schizophrenia to have psychotic and neurotic affective symptoms, but since these symptoms are lower in the hierarchy it does not affect their diagnosis of schizophrenia.

With this concept in mind, many of the other chapters make more sense. For example, Roy's overview of suicide in schizophrenia suggests that it is significantly related to other depressive symptoms. This idea also makes sense in the context of the excellent review of the psychopharmacology of depression in schizophrenia by Siris. The important take-home message here is that when correctly diagnosed, depressive symptoms in schizophrenia can be successfully treated with antidepressants.

The other theme of this book deals with the nosological issue of whether schizophrenia and affective disorders are on a continuum or represent two distinct disorders. Rogers and Winokur provide a strong case for these being two distinct disorders. Crow, as usual, provides a clever but idiosyncratic defense of the continuum hypothesis. Finally, DeLisi and Hoff provide an exhaustive review of biological markers that might, but currently do not, throw light on the dichotomy versus continuum controversy.

DANIEL J. LUCHINS, M.D.
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Living and Working With Schizophrenia: Information and Support for Patients and Their Families, Friends, Employers and Teachers, 2nd ed., by J.J. Jeffries, E. Plummer, M.V. Seeman, and J.F. Thornton. Toronto, University of Toronto Press, 1990, 148 pp., \$11.95 CDN (paper).

The family has frequently been implicated in discussions about schizophrenia. The blame-oriented research of the past and current deinstitutionalization policies combine to create a situation in which many families, who are bewildered by the behaviors of the schizophrenic relative for whom they assume the burden of primary care, are frequently kept at arm's length by the medical system and may even be denied access to the diagnosis.

Psychoeducation responds to the need of families for information about schizophrenia. Unfortunately, psychoeducational programs are not available to all who would use them, nor are all family members ready to attend available courses. This compact guide can meet the needs of those who desire to know more about schizophrenia and how they may best respond to it.

Living and Working With Schizophrenia was written in Toronto and applies equally well into the U.S. experience. This second edition of the 1982 publication includes additional sections on such topics as outcome and adopting the children of schizophrenic parents and adds an appendix briefly describing neuroleptic medications. Throughout the text, one finds updated information from recent research.

The authors include chapters describing the illness and its

hypothesized causes, the logistics of inpatient and outpatient treatment, the basics of medications, how relatives may help, outcome, support for relatives, and work and school. Particularly pertinent to the preoccupations of families are sections dealing with medication noncompliance, the use of street drugs, what happens when the supporting relatives die, and whether it is best for the schizophrenic patient to remain at home. The appendixes describe the usefulness of various agencies, the names and addresses of self-help groups in all states and provinces, descriptions of 20 neuroleptics, and a suggested reading list. The factual information provided is complemented by several first-person accounts by parents and recovering patients with schizophrenia and one essay entitled "The Doctor's Dilemma."

A major asset of this book is that it contains a great deal of valuable information while remaining readable by most, avoiding both oversimplification and condescension. The information given can assist readers in understanding and accepting the illness and thus decreasing their own anxiety and fear. It can also be used in the management of the schizophrenic patient. The utility of this book as a reference source will be valued by many readers. In addition, relatives may particularly appreciate hearing the accounts by the schizophrenic patients themselves, since their own family members may not be capable of describing their experiences as clearly. From the psychiatrist's account, they may learn to understand how the clinician may often be between a rock and a hard place when it comes to dealing ethically with both patient and family.

If this work has any shortcomings, they are related to the advantage of its brevity: some sections, including how relatives can get help for themselves, are quite brief. Fortunately, the authors open doors for the reader to get the extra help or information needed. Ideally, this recommendable book would be routinely handed out to every family member who arrives in the emergency room with a young person they no longer recognize or understand in tow. Once the diagnosis of schizophrenia is established, it is up to clinicians to make families aware of this publication if they are not in a position to educate families themselves.

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Schizophrenia: Treatment of Acute Psychotic Episodes, edited by Steven T. Levy, M.D., and Philip T. Ninan, M.D. Washington D.C., American Psychiatric Press, 223 pp., \$34.50.

This book is a good review of current knowledge about schizophrenia. This sort of information is always useful to the medical student or novice physician. Unfortunately, there is very little new information for the experienced psychiatrist or researcher. The book begins with a good description of the evolution of the concept of schizophrenia over time. The appendix at the end of chapter one is an excellent summary of diagnostic criteria. The rest of the text is similarly organized.

Chapter two gives us a clear picture of what to expect in acute psychotic emergencies. The authors could have explained treatment options better and seemed to rely on only a few sources of information for background material. It is remarkable that they mention Amytal but fail to really discuss the similar use of lorazepam. There is relatively little information regarding the legal implications of the involuntary treatment of psychiatric emergencies. Although not strictly a medical issue, this problem often occurs during crisis intervention.

A general overview of this area and citation of important cases would have made this a stronger chapter.

Proper psychological testing is important, and chapter three makes this point. The appendix of psychological tests is a good addition to the text. This section is straightforward and interesting. The only flaw in the section is that it is too brief. Further expansion on testing for organic illness would have made this portion more useful.

The review of psychopharmacology is quite good. The information on neuroleptic blood levels is up-to-date and informative. Although little new material is presented, the general information on the pharmacological treatment of schizophrenia is excellent. The bibliography from this section is very good, and the pharmacology section is well referenced.

The psychopharmacology section is followed by a chapter on neuroleptic malignant syndrome. I was pleased to see something on neuroleptic malignant syndrome in a basic text, and the authors handle the material well. The discussion of differential diagnosis is well thought out, and several good ideas about the treatment of neuroleptic malignant syndrome are provided.

The section on the treatment alliance may be a little alien to some biological psychiatrists these days. The authors give interesting reflections on the ideas of Anna Freud and Manfred Bleuler and a reasonable discussion of transference issues. Although this is not new material, we could all probably benefit from reading something like this once in a while. It adds a human touch to an area of psychiatry that is often rather sterile in its approach to treatment for psychotic people.

The discussion of milieu therapy seems too open-ended. A good description of the psychiatric care unit is given, but more references regarding the validation of this approach would have been a nice addition. Much of this section seems historical in nature and tends to be a bit philosophical. The chapter does not specifically address the needs of the acutely psychotic patient. It misses some opportunities to contrast the needs of acutely ill people to those of chronically ill individuals. Although they take a broadly philosophical approach, the authors do not take the opportunity to speculate on the effects of unique milieu situations. For example, it would be interesting to hear about the "milieu" of homeless mentally ill people and its effect on society.

Although it is not perfect, *Schizophrenia: Treatment of Acute Psychotic Episodes* is a valuable addition to the library of any clinician. Medical students and psychiatry interns may find it to be a low-key approach to important issues they deal with.

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PANIC DISORDER

Neurobiology of Panic Disorder, edited by James C. Ballenger, M.D. New York, John Wiley & Sons, 1990, 391 pp., \$96.00.

As James Ballenger notes in his preface to this fine volume summarizing what is known about the neurobiology of panic disorder, anxiety used to be thought of as more psychological than biological. Traditionally, the more severe mental disorders, such as the psychoses, were considered to be caused by a physical disorder. The milder ones, particularly anxiety, were more the province of psychotherapists; it was assumed that the etiology was mainly psychological. In Freud's later

formulations, anxiety was a signal of leakage of unacceptable, repressed thoughts and feelings and, as with most signals, was less important than the disturbed apparatus that was sending the signal. It is ironic that it is in the anxiety disorders that psychopharmacology and biological psychiatry have scored great success.

It is now clear that many agents can induce panic and cause symptoms almost identical to the natural panic attack. Successful treatment usually blocks the induced panic. With this tool, biological psychiatry has honed in on panic disorder. This volume is a comprehensive yet almost terse survey of the field.

The story is not tidy. The book documents many leads, but none has caught the brass ring yet. The reader will be left not only with much knowledge but also with anticipation to hear how this all turns out. Not all the theories can be right, or panic is incredibly heterogeneous.

We are led through no fewer than four postulated brain mechanisms for panic anxiety: noradrenergic, β -adrenergic, serotonergic, and γ -aminobutyric-acid/benzodiazepine receptor models. Individual chapters are provided by groups that have done research with each model, and the chapters are descriptions of particular studies rather than critical reviews of the field. This has its advantages. We are in the midst of data for each theory, which is far better than reading vague summaries in review articles. Sometimes, however, I wished the editor would step in and offer some aid in critically assessing these data.

For me, the heart of the book is the section on challenge strategies. I think that the center of the problem is trying to understand why lactate and other agents induce panic.

Biological psychiatry has two main divisions: psychopharmacology and neurobiology, i.e., what happens when we add an external agent to the mix and what it is in the brain that is responsible for the disorder. For me, psychopharmacology is aiming at a haystack with a needle. If we know that a drug does something important, then there must be pay dirt in figuring out how the drug works. The other side, neurobiology, is looking for a needle in the haystack. Our knowledge of how the normal brain works has, as the saying goes, exploded. We are accustomed to frequent stories in the *New York Times* about the latest dramatic finding. The links to psychopathology of all this information, however, have been minimal. With all that is going on in the brain, and it gets more complex by the hour, it seems improbable that the piece of the system you happen to study is going to be the one that gives the answer to anxiety, or schizophrenia, etc.

It is here that the lactate challenge, by far the most studied of the challenges, can be rewarding. There are just so many things that lactate can do, and thus it is possible to see which of these effects occurs during the natural appearance of panic.

Once again the story does not turn out as expected. Most researchers, I believe, expected lactate to affect the noradrenergic system in some major way, since the symptoms of anxiety seem close to a cascade of adrenergic overflow. The surprise has been that changes in heart rate, blood pressure, and pH, although they occur, are relatively modest, or else fail to explain much, and that the respiratory system appears to be where the action is.

Are we full circle to the lore we learned in medical school that a brown paper bag is a vital accessory to work in the emergency room? The chapters on this by members of the Columbia group (Sandberg, Liebowitz, Gorman, and Papp) are particularly well written and cogent. Can I say we are left breathless? The clue to the case seems to be here, but it eludes

a firm grasp. Whenever you think it is all falling into place, the facts squirm away.

Yes, hyperventilation can cause some symptoms that resemble panic, but it does not regularly cause panic in patients with panic disorder. The pH is intimately tied up with respiration, but it gets complicated. Intravenous lactate administration causes a metabolic alkalosis, but the charged ions in the periphery that bring up the pH do not get into the brain easily. Carbon dioxide, which is increased by the effect of lactate on the bicarbonate buffer system, does get into the brain easily and causes a drop in the pH. Experimentally induced panic causes hyperventilation, perhaps by the carbon dioxide getting to the chemoreceptors in the medulla, but we do not know if this means that a supersensitive carbon dioxide receptor is the cause of anxiety or a consequence.

Breathing carbon dioxide is a potent challenge, and it would fit in the supersensitive carbon dioxide receptor model. However, the hyperventilation induced by breathing carbon dioxide might induce panic by other paths.

All this attention to neurobiology must not make us forget that people, not laboratory specimens, panic and that psychological mechanisms cannot be neglected. Hyperventilation induced by carbon dioxide causes discomfort not only by its central effect on the chemoreceptors in the medulla but by the mechanical difficulty of increased muscular work. It also has cognitive meaning. Suffocation must be a basic fear, and inducing it by hyperventilation might cause panic through this psychological route.

There are other complexities in the relationship of respiration to panic beyond the scope of a brief book review. We can look forward to exciting new findings, and the reader of this book will be prepared for understanding them.

Yet another unexpected finding is the interesting work of Reiman in St. Louis, who found increased cerebral blood flow in the right parahippocampal area in patients with panic disorder who panic during lactate infusion. During the lactate-induced infusion there are large increases in cerebral blood flow in bilateral temporal poles and smaller increases in the insular cortex and the claustrum. Reiman's chapter alone is worth the hefty price of this book because he explains what positron emission tomography scanning is and where the state of the art is in handling its many problems. It seems, then, that vulnerability to panic and the actual panic attack are neuroanatomically different.

To complete the survey, the book includes a review of immunology and sleep mechanisms in anxiety. The findings here are not yet big-league concerning specifics about panic, yet these are good reviews of anxiety and the immune system and prostaglandins in the CNS.

I recommend this book for those who want to be introduced to the neurobiology of panic, surely one of the most exciting areas in biological psychiatry. The reader could skim much of the technical details to hit the high points. I recommend the book, as well, to the more specialized reader who wants an up-to-date reference. It is hard to keep up with the latest work in the diversified attack on the problem of panic anxiety. Here,

in one, manageable volume, the entire field is given in reasonable detail. One hopes that more knowledge will bring elegant simplicity. This book documents the fishing expedition that the field has undertaken.

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Clinical Aspects of Panic Disorder, edited by James C. Ballenger, M.D. New York, Wiley-Liss, 1990, 328 pp., \$96.00.

This book on panic disorder is part of a series entitled Frontiers of Clinical Neuroscience. As one might expect from the title, it is based on the medical model and oriented toward "hard" science. The editor seems to have taken care in selecting the chapter authors, and it is clear that all the authors are knowledgeable and experienced. Care was also taken in the editing process, and it seems to hold together as a book fairly well. The writing style is readable, although a little dry at times.

The book is divided into five sections. The first section, Depression, contains chapters examining the development of concepts of anxiety and panic, clinical features of panic, and biological tests attempting to differentiate the anxiety disorders. It is comprehensive and interesting; however, clinicians would probably want to read the more clinically oriented sections and skim the rest. The second section, Epidemiology, contains two chapters. The first reports on some of the Epidemiologic Catchment Area study results for panic disorder, and the second chapter reviews epidemiologic studies from different parts of the world relating to panic and anxiety. Both chapters are competently written. The third section, Cardiovascular Studies, has three approaches. The first examines the microphysiology of patients with panic disorder and determines that it resembles that of normal subjects. The second examines the evidence for panic being a risk factor for cardiovascular disease in panic patients. The data here are preliminary and mixed, with no final conclusions possible at this time. Finally, the incidence of panic disorder presenting as atypical chest pain is examined. (Many patients with atypical chest pain have panic disorder.) The fourth section, The Relationship Between Panic Disorder and Major Depression, deals with the difficult area of nosology. Different chapters delineate the tendency toward comorbidity of the two disorders, their similarity in terms of biochemical tests, and their similarity in response to certain types of treatment. The last section of the book is devoted to treatment issues. Dealt with here are bread-and-butter issues of psychopharmacological treatment of depression.

Overall, this book has value to clinicians and researchers interested in the area of panic disorder.

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Reprints of Book Forum reviews are not available.

Letters to the Editor

Tricyclics and Heart Failure

SIR: During the past decade the effect of tricyclic antidepressant medications has been examined in seven studies using radionuclide angiography in 89 patients with impaired left ventricular function (1). Although the rate of orthostatic hypotension due to tricyclics increases in this population, the conclusion in these studies has been that tricyclics, at therapeutic concentrations, do not have a deleterious effect on left ventricular function (1). The sporadic case reports of congestive heart failure associated with tricyclics have occurred in conjunction with unusually high levels of hydroxy metabolites (2). We now report the case of a patient with major depression and preexisting cardiovascular disease whose cardiac failure worsened when he was taking tricyclic antidepressants.

Mr. A, a 79-year-old man, was admitted to the hospital with his fourth episode of major depression. Medical evaluation revealed an intraventricular conduction delay of 0.12 seconds, an ejection fraction of 47% by radionuclide angiography, and mild pedal edema. He consented to enter a double-blind, crossover medication study comparing the cardiovascular effects of doxepin to those of nortriptyline. Initially, he received nortriptyline, up to a dose of 75 mg/day by day 5. On day 9 it was noted that he had a prolonged QRS interval of 0.18 seconds, and the medication was discontinued as indicated by the protocol. His plasma level of nortriptyline at that time was 120 ng/ml, with E- and Z-10-hydroxynortriptyline levels of 162 and 41 ng/ml, respectively. A repeat ejection fraction was 39%. Evaluation for myocardial infarction was negative. On the fifth day after stopping nortriptyline, his plasma level was zero, and the QRS interval had returned to baseline. The ejection fraction was 50% 11 days after stopping nortriptyline.

Doxepin was begun, and the dose was gradually raised to 260 mg/day without increased conduction delay. However, during the 20 days he took doxepin, Mr. A gained 6 lb, had increased pedal edema, and developed paroxysmal nocturnal dyspnea. His ejection fraction was 34%, and his plasma level of doxepin plus desmethyldoxepin was 192 ng/ml. Myocardial infarction was ruled out. He continued taking doxepin for another week, and a repeat ejection fraction was 34%, with a plasma level of 307 ng/ml. Doxepin was discontinued. Over 6 days the patient's weight decreased 5 lb, the pedal edema diminished, the paroxysmal nocturnal dyspnea resolved, and the ejection fraction was 44%.

This patient's ejection fraction decreased considerably when he took two different tricyclic antidepressants and returned to baseline after the medications were discontinued, which is highly suggestive of an effect of the medications. With respect to nortriptyline, the Z-10-hydroxy metabolite has been shown to diminish cardiac inotropy, whereas the E-10-hydroxy metabolite has not (3). While the patient's Z-10-hydroxy metabolite level was somewhat greater than expected (3), the factors mediating the changes in cardiac inotropy in this case remain unclear.

This case highlights the difficulty in deciding when to declare a drug "safe" (4). Clearly, failing to establish a negative inotropic effect for tricyclics among 89 depressed patients with impaired left ventricular function does not mean that such an effect does not exist (5). Although the vast majority of the patients who were studied had no worsening of their inotropic function, the 90th patient did. As this report indicates, safety is not absolute. The clinician is obliged to keep a watchful eye for this clinically significant, if unusual, cardiovascular effect.

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Recent Fluoxetine Treatment and Complications of Tricyclic Therapy

SIR: Serious adverse effects of combining fluoxetine and tricyclic antidepressants have been noted (1) and are presumably related to fluoxetine's inhibition of the metabolism of tricyclics, producing more than twofold increases in plasma tricyclic levels (2-4 and *Physicians' Desk Reference*, 44th edition). Elevated tricyclic levels associated with this combination decrease very slowly following discontinuation of fluoxetine (3). The long elimination half-lives of 2-3 days for fluoxetine and 7-9 days for its active metabolite norfluoxetine ensure that active drug or metabolite persists in the body for weeks after discontinuation of fluoxetine (*Physicians' Desk Reference*, 44th edition). Physicians should be alert to the possibility that recent treatment with fluoxetine may significantly influence metabolism of subsequently prescribed tricyclic antidepressants, requiring special dosage adjustments over time to establish and maintain therapeutic levels of the tricyclics and clinical response.

Ms. A, 46 years of age, was hospitalized with major depressive disorder that had been unresponsive to fluoxetine, 20-40 mg/day, for 3 months prior to admission. Fluoxetine was discontinued, and after 1 week nortriptyline was

started. At a dose of 50 mg/day, her weekly steady-state plasma nortriptyline levels fell from 111 to 91 to 74 ng/ml (therapeutic range=50–150 ng/ml) as initial improvement was not sustained. Triiodothyronine, 25 µg/day, was added as a potentiating agent. A week later her plasma nortriptyline level had fallen to 50 ng/ml, and the dose of nortriptyline was increased to 75 mg/day. A week later, with a plasma level of nortriptyline at 115 ng/ml, the patient had improved and was discharged.

Ms. B, 41 years of age, was hospitalized with major depressive disorder that had not responded to 6 months of treatment with fluoxetine, 20–40 mg/day, which had been discontinued 1 week before admission. Ten days after admission she was started on nortriptyline. At a dose of 75 mg/day, her weekly steady-state plasma nortriptyline levels fell from 131 to 119 to 72 ng/ml. Triiodothyronine, 25 µg/day, was added as a potentiating agent. The dose of nortriptyline was increased to 100 mg/day, and a week later, with her plasma nortriptyline level at 126 ng/ml, she had improved enough to be discharged.

In both cases, triiodothyronine was added as a potentiating agent after poor response to at least 3 weeks of treatment with nortriptyline at therapeutic levels. When the pattern of falling nortriptyline levels was noted, the nortriptyline dose was increased. In retrospect, it probably would have been more reasonable to increase the nortriptyline dose to maintain plasma levels around 100 ng/ml without adding triiodothyronine.

The scenario in which patients not responding to fluoxetine are switched to tricyclics is not unusual, since fluoxetine has become the most commonly prescribed antidepressant in the United States. These two cases suggest that recent fluoxetine treatment may influence tricyclic metabolism and hence dosage needs.

Initially, plasma tricyclic levels may be higher than they would be otherwise, because of fluoxetine's lingering inhibition of tricyclic metabolism. Thus, prescribing without monitoring plasma levels of tricyclics may be associated with more side effects and/or poor response. During the next several weeks, plasma tricyclic levels may fall as fluoxetine's inhibition of tricyclic metabolism dissipates. Tricyclic dosage may need to be increased to maintain therapeutic plasma levels and achieve clinical response. Failure to increase the dosage of tricyclic may lead to some patients' being falsely labeled as tricyclic nonresponders.

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Serum Sickness Induced by Fluoxetine

SIR: Fluoxetine is a potent serotonin reuptake inhibitor (1) widely used in current practice. To our knowledge, only one

case report of probable serum sickness induced by fluoxetine has been published (2). We describe a case in which a "rechallenge" was done.

Ms. A, a 22-year-old mother, consulted us for postpartum depression. She was in good physical health, but she was known to be sensitive to nortriptyline (ictus) and phenytoin (rash). She was prescribed fluoxetine, 20 mg/day, but ceased taking it after 3 months for no apparent reason. Three months later, lithium carbonate was started because she had developed cyclothymic features. Trazodone and multiple benzodiazepines (bromazepam, flurazepam, lorazepam, and alprazolam) were added by various physicians because of her lack of response.

Ms. A was hospitalized 1 month later because of a suicide attempt. Trazodone, flurazepam, lorazepam, and alprazolam were stopped. Fluoxetine was reintroduced at a dose of 20 mg/day. Three days after fluoxetine was started, she developed sore and swollen nodes, and the day after that her temperature reached 38.5 °C. A morbilliform rash appeared on the fifth day. She complained of myalgia and fatigue and was feeling anorexic. A viral or bacterial infection was suspected and a complete investigation was started. Every test came back with negative results. Fluoxetine and lithium were stopped within 4 days and all symptoms disappeared. At that time, the phenomena seemed to have an infectious origin and not to be drug-related.

Because Ms. A was still depressed, fluoxetine was restarted the next week. Five days later a generalized rash appeared, accompanied by symptomatic postural hypotension and painful lymphadenopathy. Fluoxetine-induced serum sickness was diagnosed, and fluoxetine was stopped for good. The rash and pruritus took several weeks to disappear completely. She was treated with antihistamines and topical glucocorticoids.

Laboratory assessment revealed a small elevation in hepatic enzymes, but within the normal range. Ms. A's WBC count dropped to 2,800/mm³ in 28% of the samples during the rechallenge with fluoxetine but rose rapidly after the drug was stopped. Hemoglobin, platelets, and sedimentation rate were unchanged, as were thyroid function and serum creatinine levels. There was no eosinophilia.

Serum sickness results from a hypersensitivity reaction mediated by the deposition of immune cell complexes (3). The main symptoms are rash, fever, myalgia, arthralgia, and lymphadenopathy. The kidneys, lungs, and heart can be involved. Rare cases of meningoencephalitis have been described. Laboratory assessment can show leukopenia or slight leukocytosis, eosinophilia, and elevated sedimentation rate. Complement levels may be low. Proteinuria and hematuria can appear, but there is no specific finding.

Treatment consists of removing the causal agent. Urticarial symptoms may respond to antihistamines or, if severe, to corticosteroids. Inflammation can be reduced by anti-inflammatory agents.

The case we have presented showed many features common to serum sickness, and the rechallenge with fluoxetine leaves no doubt about the etiology. Moreover, the complete workup demonstrated no infectious process to explain the symptoms.

A personal communication from Eli Lilly and Company (February 1991) indicated that there have been some isolated case reports of fluoxetine-induced serum sickness; as of Sept. 30, 1990, 32 cases in 2.5 million patients treated with fluoxetine had been reported. Even if this phenomenon is potentially very serious, its rare occurrence should not prevent us from using fluoxetine in clinical practice.

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Penile Anesthesia Associated With Fluoxetine Use

SIR: Fluoxetine, though beneficial in the treatment of depressive disorders, may still have an incomplete side effect profile. We report an unusual side effect of fluoxetine when it was used in a patient with depression.

Mr. A, was a 47-year-old man who had been chronically depressed for 6 years, with several acute exacerbations. His general state was one of low energy, bad sleep, and no hedonic tone. His acute episodes were accompanied by vague suicidal ideation. He had had trials of small amounts of antidepressants, which were terminated because of urinary retention.

Mr. A reported no difficulties with erection, ejaculation, or sexual pleasure during his usual depressed periods, but he was unable to obtain an erection and had a loss of libido during his depressive "potholes." This experience was confirmed by his wife.

A mental status examination revealed the patient to be a depressed man, neatly dressed, who was slow and precise in expressing himself and maintained a downcast demeanor throughout the interview. His thoughts and feelings dealt with his present state of helplessness and worthlessness and his powerlessness in the face of depression. There was a strong history of depression in two generations of the family.

It was felt that Mr. A met the criteria for recurrent depression and dysthymic disorder. He was placed on a regimen of 20 mg/day of fluoxetine. After approximately 4 weeks, with no response, the dose was raised to 40 mg/day. Finally, the dose was raised to 60 mg/day, and over a 4-week period the patient exhibited an "amazing" remission of his depressive symptoms. He said, "For the first time in many years, I feel like I'm really alive." Initially, there were no side effects. Beginning during the second week at 60 mg/day of fluoxetine, Mr. A began to complain of penile anesthesia. He reported that he desired intercourse with his wife and could get an erection, but he experienced numbness of the glans penis. He was eventually able to ejaculate with effort. This caused him a great deal of distress and did not disappear over the ensuing months.

The dose of fluoxetine was lowered to 40 mg/day, with no loss of antidepressant effect but no improvement of the penile anesthesia. At the same time, Mr. A was started on cyproheptadine, 4 mg each morning (1). Against medical advice, Mr. A stopped taking fluoxetine, and his depressive symptoms returned within 2 weeks. His penile sensitivity also returned during this period, and he asked to be given another antidepressant.

To my knowledge, penile anesthesia has not been reported as a side effect of antidepressant therapy. Pollack and Rosen-

baum (2), in a review of the diagnosis and treatment of antidepressant-induced side effects, did not cite this difficulty.

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Effect of Fluoxetine on Patients With Multiple Sclerosis

SIR: We read with interest the report by W. Nicholson Browning, M.D. (1) of a patient with multiple sclerosis who had an apparent exacerbation of symptoms within 10 hours after taking fluoxetine. In the past 2 years we have treated 20 patients with multiple sclerosis who have been placed on fluoxetine regimens for depression or emotional incontinence, with follow-up periods ranging from 2 to 21 months. We have seen an excellent response to fluoxetine, often within several days, and few if any side effects in all 20 patients. In fact, several of our patients have reported improvement in neurological symptoms, such as ataxia, slurred speech, and dysphagia, which they attribute to fluoxetine. In no case have any neurological symptoms been temporally related to the administration of fluoxetine. In contrast, we and others (2) have found tricyclic antidepressants to be poorly tolerated in this patient population.

Considering the relapsing and remitting nature of multiple sclerosis, it is tempting to infer erroneously a causal relation between a variety of stimuli and the occurrence of neurological symptoms in this population. It is likely that the response of Dr. Browning's patient was idiosyncratic or a chance association. We consider fluoxetine to be an effective and relatively safe treatment for emotional incontinence and depression in patients with multiple sclerosis.

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Association of Fluoxetine With Suicidal Ideation

SIR: We read with interest the letter by Cynthia E. Hoover, M.D. (1) that provided a follow-up of a patient she had described in an earlier issue of the *Journal* (2) who developed suicidal ideation while taking fluoxetine. According to the follow-up information, Dr. Hoover concluded that fluoxetine did not have any relation to the development of suicidal ideation in this case because "intermittent extreme suicidal idea-

tion of the same quality occurred in this patient when he had levels of imipramine plus desipramine between 241 and 432 mg/dl.⁹ We would like to propose an alternative explanation for her clinical findings. It is quite likely that the patient developed treatment-related suicidal ideation when taking both fluoxetine and imipramine and that the relationship was not merely coincidental as Dr. Hoover postulated.

Damluji and Ferguson (3) described four patients who developed suicidal ideation when taking desipramine. All four patients subsequently developed suicidal ideation when taking other antidepressants (two were taking amoxapine, one trazodone, and one nortriptyline). Thus, it is quite likely that there is a small minority of patients who are sensitive to developing a paradoxical worsening of depressive symptoms and suicidal ideation with more than one antidepressant, as Dr. Hoover described.

Furthermore, one of the arguments that Dr. Hoover advanced as supporting the lack of an association between suicidal ideation and fluoxetine was the retrospective study of 1,017 depressed patients by Fava and Rosenbaum (4). However, although they emphasized the lack of statistically significant differences between the suicidal ideation associated with fluoxetine alone and that associated with other antidepressants, their data did show an association of suicidal ideation with fluoxetine, since 12 patients (eight taking fluoxetine alone and four taking a combination of fluoxetine and tricyclic antidepressants) developed suicidal ideation after the initiation of treatment. Only a large prospective, double-blind study designed to address this issue can definitively resolve this question.

Meanwhile, clinicians should be aware that suicidal ideation can occur in association with fluoxetine treatment in a small minority of patients (5).

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Potential Interaction Between Warfarin Sodium and Fluoxetine

SIR: Recently, on our psychiatry consultation and liaison service, we were asked to see a woman with recurrent depression and a history of deep vein thrombosis. She had been initially started on fluoxetine and was secondarily started on warfarin sodium. The patient presented with severe bruising of both lower extremities. We were asked to investigate the case to determine whether a drug interaction had produced the problem.

On consulting the *Physicians' Desk Reference* (44th edition, pp. 905-908), we discovered that warfarin sodium and fluoxetine are bound to the same plasma protein. A review of world

literature databases failed to yield a report of a drug interaction between fluoxetine and warfarin sodium that had produced a bleeding disorder. Scrutiny of our patient's case did not produce evidence that this had occurred. A retrospective analysis of six additional cases was performed; none of these patients had required adjustment of their dose of warfarin sodium while they were taking fluoxetine. Correspondence with Eli Lilly and Company, the manufacturers of fluoxetine, revealed that as of June 30, 1990, approximately 2,382,000 patients had received the drug. In this population there were only 24 reports of an increase in bleeding time, a coagulation disorder, or an increase in coagulation time.

It is our hope that this brief report alerts other investigators to be aware of the possible drug interactions of fluoxetine and warfarin sodium.

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Fluoxetine and Parkinsonism in Patients Taking Carbamazepine

SIR: Fluoxetine alone or in combination with neuroleptics has been reported to cause parkinsonism in some patients (1, 2). We report two patients who were taking carbamazepine and developed moderate to severe parkinsonism after fluoxetine was added.

Mr. A, 74 years of age, known to have bipolar disorder, had taken carbamazepine, 200 mg b.i.d., for 12 months before he was admitted to the hospital for a major depressive episode without psychotic features. On physical examination he was noted to have a slight symmetrical hypertonia of the upper extremities, which caused no complaints. His carbamazepine serum concentration was 6.0 mg/liter. He was started on fluoxetine, 20 mg/day. On the third day of treatment, he developed severe cogwheel rigidity (elbows, wrists, neck), a mask-like face, and a typical parkinsonian gait, and his mood worsened. His carbamazepine level at this time was 6.5 mg/liter. Fluoxetine was discontinued, and the anticholinergic drug dextenidine was started. Seventeen days later, only a slight hypertonia of the arms was observed.

Ms. B, a 53-year-old patient with schizoaffective disorder, bipolar type, was admitted to the hospital for a major depressive episode without psychotic features. On admission she was taking thioridazine, 275 mg/day. She had never been known to have parkinsonism. She was given carbamazepine, 200 mg b.i.d., and had a serum concentration of 7.0 mg/liter. The dose of thioridazine was decreased to 200 mg/day. Twenty-four days later, fluoxetine, 20 mg/day, was added and thioridazine was stopped. Nine days later Ms. B developed cogwheel rigidity of moderate severity and a mask-like face. Her carbamazepine serum concentration at this time was 7.4 mg/liter. Her mood gradually improved, whereas her parkinsonism remained.

The time sequence of events strongly suggests that the relation between the onset of parkinsonism and the addition of fluoxetine to carbamazepine was a causal one. The mechanisms remain speculative but are probably related to an acute effect of fluoxetine: blockage of presynaptic serotonin (5-HT) reuptake with resultant increased 5-HT availability at the syn-

aptic cleft. Interestingly, carbamazepine has also been reported to increase brain 5-HT function (3). Induction of parkinsonism by lithium and amelioration of parkinsonism by 5-HT antagonists provide additional arguments for a role of 5-HT in this drug-associated disorder.

In humans, the substantia nigra appears to contain the highest concentration of binding sites for paroxetine, a selective 5-HT reuptake inhibitor (4). Serotonergic projections from the mesencephalic dorsal raphe to the ipsilateral nigra, mainly the pars compacta, have been demonstrated, and a consistent body of evidence indicates a direct inhibitory influence of this system upon the dopaminergic nigrostriatal tract (5).

Clinical observations and neuroscientific and pharmacological data suggest that any drug that potentiates effects of 5-HT, presumably by inhibiting dopaminergic nigrostriatal projections, may precipitate parkinsonism, especially when combined with neuroleptics or other 5-HT-enhancing drugs or when used in patients with subclinical or mild parkinsonism. If this is true, it has important implications for everyday psychiatric clinical management.

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Buspirone Augmentation of Fluoxetine in a Depressed Child With Obsessive-Compulsive Disorder

SIR: Paul J. Markovitz, M.D., Ph.D., and associates (1) reported on their success in using buspirone for patients with obsessive-compulsive disorder who had not responded to either fluoxetine alone or other medications. The following is a case report of a child who, having failed to respond to fluoxetine, went on to show marked clinical improvement following the addition of buspirone.

Ann, an 11-year-old girl with a 4-year history of obsessive-compulsive disorder and a 6-month history of depression, was evaluated because of her increasing destructive behavior in school and at home. She demonstrated a decline in school functioning, school refusal, and social withdrawal. Because of the risk of her hurting her parents and sibling, she was psychiatrically hospitalized. At the time of her admission, the results of a physical examination and a laboratory workup, including CT scan and EEG, were normal. Her score on the Childhood Depression Rating Scale

was 69. She was diagnosed as having an obsessive-compulsive disorder with a major depressive disorder.

No aggressive behavior was noted during the hospitalization, although the severity of her obsessive-compulsive disorder became more apparent. She was started on imipramine for her depression, and the dose was increased to 150 mg/day. Her blood level at this time was 160 ng/ml. Due to an orthostatic standing pulse greater than 150 bpm, imipramine was stopped and she was given fluoxetine. The dose of fluoxetine was increased to 60 mg/day, and her depression decreased. At the time of discharge, her score on the Childhood Depression Rating Scale was 37.

One month after discharge Ann was seen again, and it was noted that her obsessive-compulsive behavior (characterized by ritualistic thinking, avoidance of social situations, and a marked preoccupation with dirt) had worsened, as had her depression. Her score on the Childhood Depression Rating Scale was 61, and her score on the Maudsley Obsessive-Compulsive Inventory was 17. Intermittent aggression was noted when her parents attempted to prevent her rituals. Because of the side effects she had experienced with imipramine, it was decided to not try clomipramine. Augmentation of the fluoxetine was considered, and trazodone was begun. Within 24 hours, the patient complained of marked sedation. Trazodone was discontinued, and buspirone was started at 10 mg/day and increased to 30 mg/day over a 3-week period. At a 4-week follow-up, her depression score was 28 and her obsessive-compulsive score was 9. The parents noted marked improvement in her affect, with a decrease in depression, and improvement in obsessive-compulsiveness, with a general decrease in ritualistic practices. She returned to school and continued to do well 6 months after starting the combination of medications.

Childhood obsessive-compulsive disorder has been reported with increasing frequency. There are several reports indicating the use of clomipramine and, most recently, fluoxetine for these patients (2-4). To our knowledge, despite studies that have identified refractory obsessive-compulsive disorder in children and adolescents, there are no studies suggesting therapeutic strategies (5). Our success with buspirone supports Dr. Markovitz and associates' observations in adults and lends credence to the notion of augmenting fluoxetine with buspirone in children with obsessive-compulsive disorder. Much work needs to be done, but it appears that this combination is safe and should be considered for children with this disorder who are treatment-resistant.

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Possible Induction of Psychosis by Buspirone

SIR: Buspirone, a nonbenzodiazepine anxiolytic, has been implicated in several clinical reports (1-3) in the possible induction of panic attacks and mania. The following case report describes the development of psychosis in a patient treated with buspirone.

Ms. A was a 52-year-old woman with schizotypal personality disorder and a history of one episode of major depression 4 years before treatment with buspirone. At baseline she had occasional ideas of reference but was never frankly delusional. She had been treated in the past with low doses of neuroleptic for transient suspiciousness but was reluctant to continue even on an intermittent basis because of the risk of tardive dyskinesia. Her major complaint was mild, persistent anxiety without any evidence of clear psychotic symptoms. She had stopped taking a neuroleptic 2 months before she agreed to a trial of buspirone, 5 mg t.i.d.

Seventy-two hours after the first dose of buspirone, Ms. A became floridly delusional in the absence of mood disturbance or agitation and insisted that her neighbors were conspiring to kill her. She was instructed to stop buspirone and begin thiothixene, 5 mg/day. Within 48 hours of stopping buspirone, her psychosis completely resolved, and she then reported that she had not actually taken any thiothixene. The sudden emergence of frank psychosis in this patient, who had no history of delusions, shortly after she took buspirone and the prompt resolution of psychosis upon discontinuation of the drug suggest possible induction of psychosis by buspirone.

Buspirone, the only licensed azaspirone anxiolytic, is a serotonin 5-HT_{1A} partial agonist that may mediate anxiolysis by inhibiting the spontaneous firing rate of 5-HT neurons in the raphe and decreasing 5-HT turnover in the striatum (4). Like many antidepressants, buspirone down-regulates cortical 5-HT₂ binding sites (4). Buspirone can also enhance dopamine neurotransmission by acting as an antagonist at presynaptic dopamine receptors (4). D'Mello et al. (5) reported that buspirone was effective in reversing neuroleptic-induced akathisia, presumably by increasing brain dopamine activity. It is theoretically possible that buspirone exhibits psychotomimetic effects by enhancing dopamine neurotransmission in certain patients. To date, the drug manufacturer, Bristol-Myers Squibb, has received a total of eight reports of psychotic reactions (Evan Demestihis, M.D., personal communication, May 1, 1991). Although anecdotal reports can only suggest the possibility of buspirone-induced psychosis, one would expect psychosis-prone individuals such as the patient I have described to be more vulnerable to the dopaminergic effects of a drug and thus at higher risk for psychotic reactions.

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Possible Interaction Between Clozapine and Lorazepam

SIR: We report two cases that illustrate a possible synergistic, pharmacodynamic interaction between clozapine and lorazepam.

Ms. A, a 33-year-old woman weighing 45 kg who had schizoaffective disorder, was treated with clozapine because of severe extrapyramidal side effects when she took typical antipsychotics. She was started on clozapine, 50 mg/day, and the dose was titrated to 100 mg/day over 9 days. She had taken 100 mg/day for 2 days when she became acutely agitated. She was taking no other medications. She was given lorazepam, 2 mg i.m., and 95 minutes later she had marked sedation, excessive sialorrhea, and ataxia (she required the assistance of two staff members in order to walk) and was unresponsive to verbal stimuli. Approximately 2 hours later she was alert. Previous administration of lorazepam, while she was taking trifluoperazine, had produced calming without sedation. The patient has not been rechallenged with lorazepam.

Mr. B, a 48-year-old man weighing 49 kg who had refractory schizophrenia, was started on clozapine, 50 mg/day, and the dose was titrated to 100 mg/day over 13 days. His concurrent medications were haloperidol, 5 mg/day; benztropine, 2 mg/day; multivitamins; and laxatives. Haloperidol and benztropine were being decreased while clozapine was being increased. After receiving 100 mg/day of clozapine for 6 days, Mr. B became acutely agitated and was prescribed lorazepam, 1 mg p.o./i.m. three times a day. He received three oral lorazepam doses over 24 hours. The following day, he was noted to be lethargic, pale, drooling excessively, and ataxic and required the assistance of two staff members to walk. All medications were stopped, and the patient was placed on bed rest. Two hours later he was alert. The following day, clozapine was restarted and lorazepam was discontinued. Prior administration of lorazepam, while the patient was taking haloperidol, had produced calming without sedation. Rechallenge with lorazepam, while he was taking clozapine, 350 mg/day, produced calming without sedation.

In both patients, laboratory values and vital signs did not reveal any clinically significant abnormalities. Sedation is a common adverse effect of clozapine, occurring in 34% of patients (1). Tolerance may develop with continued treatment at stable doses. Grohmann et al. (2) described four cases of clozapine-benzodiazepine interactions in which the patients had severe sedation, hypersalivation, hypotension, toxic delirium, collapse, loss of consciousness, and respiratory arrest. These

effects occurred within 1–2 days of starting clozapine. The reports are confounded by the use of multiple, simultaneous, long-acting benzodiazepines preceding high starting doses of clozapine. We describe patients who received lorazepam as the sole benzodiazepine following lower, recommended starting doses of clozapine. Our patients did not demonstrate marked sedation or severe hypersalivation while receiving clozapine without benzodiazepines or benzodiazepines with typical antipsychotics.

These cases suggest a clinically significant, synergistic pharmacodynamic interaction between clozapine and lorazepam. We recommend cautious use of benzodiazepines when initiating clozapine treatment.

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Adverse Reaction to Generic Alprazolam

SIR: I would like to report an adverse reaction to generic alprazolam manufactured by Apotex, which became available in drug stores in Manitoba on Jan. 1, 1991.

Ms. A, a 56-year-old woman in good general health, had been maintained on alprazolam (Xanax), 0.5 mg q.i.d., since 1985 with complete control of severe panic disorder. In mid-January 1991 she had her prescription refilled and was dispensed the generic form of alprazolam. She began taking this and the next day experienced a sudden recurrence of her panic disorder. She was intensely anxious all the time, experienced a number of panic attacks per day, and had night sweats, nausea, and chest pain. Thinking there might be a problem with the generic form of her medication, she talked to her pharmacist, and he gave her a supply of Xanax and told her to start taking it again. After she took 0.5-mg doses of Xanax at 9:00 a.m. and 1:00 p.m. the next day, her symptoms remitted completely. She contacted me by telephone 2 days later to report these events.

Ms. A had had no apprehension about switching to the generic form of alprazolam and derived no secondary gain from the incident; therefore, her reaction does not appear to have had a psychological cause. She has continued in full remission on a regimen of Xanax, 0.5 mg q.i.d., for 4 months.

This patient declined to start taking generic alprazolam again for determining blood levels, and no other similar incidents have come to my attention. Therefore, no conclusions can be reached about the mechanism of the patient's reaction. However, since alprazolam is widely prescribed, physicians should be aware that when patients are switched to the generic form, they may react as if it is pharmacologically inert. Any similar observations should be reported.

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SPECT Technique for Visualization of Cerebral Dopamine D₂ Receptors

SIR: We present data on the applicability of brain single photon emission computed tomography (SPECT) with [¹²³I]pyrrolidinemethylbenzamide (IMBZ), a specific D₂ receptor ligand with a B_{\max} of 373 ± 51 fmol/mg protein and a K_d of 3.1 ± 0.6 nM (1, 2).

The aims of the studies we conducted were 1) visualization of D₂ dopamine receptor density, 2) relative quantification of D₂ receptors, 3) determination of differences in D₂ receptor densities in the brains of healthy control subjects and schizophrenic subjects, 4) investigation of changes in D₂ receptor densities in drug-free and neuroleptic-medicated schizophrenic subjects and also 5) correlations between D₂ receptor density and neuroleptic dosage, and 6) possibly, differentiation of subtypes of schizophrenia by quantitatively or qualitatively different D₂ receptor densities.

Forty probands (29 male) consented to participate; 27 were schizophrenic (DSM-III-R), eight of whom were drug free. Psychopathology was rated with the Brief Psychiatric Rating Scale and the Clinical Global Impression scale. A single-head, computer-connected ECT gamma camera (Siemens) was used for the brain SPECT. Data acquisition was started 40 minutes after intravenous injection of 5 mCi (185 MBq) of [¹²³I]IMBZ. Previously, no difference in results for three volunteers was registered at 40 or 120 minutes after injection. For estimating D₂ receptor density, ratios were calculated by mean counts per pixel of standardized regions in transverse slices of 19.5-mm thickness of the striatum over the ipsilateral frontal cortex (3).

The average ratios of D₂ receptor densities of the control subjects (1.76) and the unmedicated schizophrenic subjects (1.68) did not differ significantly but were significantly higher ($p < 0.001$, t test) than that of the schizophrenic subjects taking neuroleptics (1.39) (mean dose = 1662 ± 1010 chlorpromazine equivalents, mean BPRS score = 44.89 ± 13.00 , and mean CGI score = 4.31 ± 0.94), indicating D₂ receptor blockade. Differences from PET data (4) may be due to the different methodology.

A correlation between increase in neuroleptic dosage and decrease in average receptor ratio was established for doses over 800 chlorpromazine units ($r = 0.64$, $N = 15$, $p < 0.01$).

One patient, who consented to consecutive scans at doses of 0, 890, 2750, 4500, and 4800 chlorpromazine units, seemed to show development of D₂ receptor hypersensitivity over 63 days (5). The average ratios of 1.42, 1.38, 1.34, 1.26, and 1.55, respectively, for chlorpromazine units ranging from 800 to 4800 (haloperidol droplets) demonstrate receptor blockade, the increase possibly a hypersensitivity of the receptors.

In all control subjects we registered a significantly lower ratio of D₂ receptor density in the left hemisphere (right to left = 1.80:1.72; $p < 0.006$). The drug-free schizophrenic subjects (mean BPRS score = 45.25 ± 6.86 , mean CGI score = 4.13 ± 0.99) presented only a modest hemispherical difference (right to left = 1.72:1.66; $p < 0.27$). On a 95% level they also showed lower ratios of D₂ receptor density than in the control subjects' right hemispheres.

Dividing the schizophrenic subjects into two groups according to whether their BPRS scores were below or above 40 yielded no significant differences in receptor densities.

Our results indicate that sufficient quality of IMBZ imaging of D₂ receptors is possible with single-head SPECT, facilitating its widespread use. Additionally, the method may serve to control cerebral D₂ receptor density or (neuroleptic) blockade and so complement plasma-level data in therapy evaluation and possibly identify receptor hypersensitivity. Furthermore, our

data indicate strong interindividual variations, which so far preclude routine differentiation of subtypes of schizophrenia. We suggest further research in this field.

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Reporting of Child Abuse

SIR: Once thought to be literally a one-in-a-million phenomenon, child abuse is now seen as affecting 20%-70% of all psychiatric patients (1). Although a considerable percentage of patients in most diagnostic groups, including those with schizophrenia, affective disorders, and anxiety disorders, probably have histories of abuse in childhood, studies on all of these diagnostic groups published in our best psychiatric journals still fail to report the percentage of their patient samples who have experienced such abuse. We know that child abuse is common, but we are still acting as if it were rare. If child abuse is harmful and is thought to affect 20%-70% of all psychiatric patients, researchers should report the percentage of their patient samples who have histories of child abuse. If this is done routinely, perhaps we will eventually discover the effect of child abuse on neurotransmitters and the percentages of patients in various diagnostic groups who are suffering posttraumatic sequelae. Since most researchers are not used to reporting histories of child abuse in their study groups, editors will probably have to make this a prerequisite for publication.

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Case Involving Issues Similar to Those in *Osheroff*

SIR: The case of *Osheroff v. Chestnut Lodge* involved an allegation that failure to use psychopharmacologic interven-

tions for a man with depression may have represented negligent psychiatric care. Experts for the plaintiff alleged, *inter alia*, that the decision not to use medications represented a bias, influenced by anachronistic dynamic concerns about intruding on the psychotherapy. The case was settled out of court, so the legal ramifications of the issue were not resolved. Nonetheless, the case raised a large debate over the relative merits and relevance of psychodynamic psychotherapy and psychopharmacology and the possible effects that the choice of one modality over the other may have on the patient.

We recently saw a patient whose case offers a commentary on the issues raised by *Osheroff*.

Dr. A was a 32-year-old woman who had graduated from a prestigious undergraduate university and received her medical degree from a local medical school. During medical school she was diagnosed in a psychopharmacology clinic as having bipolar disorder. She was seen monthly by a psychiatrist for approximately 15 minutes and received lithium carbonate. Psychotherapy was neither offered nor recommended, according to the patient. After being placed on the lithium regimen, the patient had neither manic nor depressed episodes.

After graduation, Dr. A was not hired for the position that she expected. She had not made other plans and suddenly found herself without financial means. She refused offers of financial assistance from her mother. She moved out of her apartment and took residence at a local shelter for the homeless. When she subsequently got a haircut at a moderately expensive hairdresser, she failed to pay for the service. She told the manager that she had discovered that the wallet containing her remaining cash had been lost. The patient's ability to convince the manager of her intention to pay the bill was limited by her lack of a job or a home. When the police came, she became uncooperative and angry. She was arrested on misdemeanor charges. Because of her admission that she was taking lithium and her unusual story, she was transferred to the locked ward of a psychiatric hospital.

When she was examined at the hospital, Dr. A exhibited no symptoms of acute mania, hypomania, or serious depression. However, she had a considerable number of narcissistic and dependent issues that appeared to contribute to her difficulties in making contingency plans and her failure to negotiate successfully with the business owner and police officers. The dynamic issue of "thumbing her nose" at her mother, among other issues, seemed apparent during her hospital stay.

Might psychotherapy have helped this woman? She left the correctional system with a considerable chance of having a criminal record that might significantly impair her future employability. While there exist no guarantees that she would have been receptive to psychotherapy or that it would have been helpful, the psychotherapeutic possibilities for this patient to learn foresight, plan for her life, and adapt to her illness were foreclosed when psychotherapy was not even offered. Especially considering that the underlying mood disorder did not appear to lead to the arrest and its attendant results, the dramatic and clearly damaging outcome of this case is striking.

We offer the case as an opportunity for reflecting on a possible new bias against psychotherapy that is conveyed in the rush to medicate. This letter is not intended to suggest that the patient's psychiatrists committed malpractice. However, the

case represents to us an example of a situation in which psychotherapy might have been an important form of treatment.

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Delayed Onset of PTSD: Delayed Recognition or Latent Disorder?

SIR: Persistence of symptoms of posttraumatic stress disorder (PTSD) for many decades following trauma is a well-known phenomenon (1, 2). Several reports suggest that onset of the disorder may be delayed for an equivalent length of time in some cases (3, 4). This raises the question of whether such delay represents latent or merely unrecognized PTSD. The following case suggests the former.

Mr. A was a 63-year-old Korean War veteran referred for psychiatric evaluation. He had always viewed his years in the military as uneventful, except for an incident near the end of his tour of duty when he strangled several Korean soldiers while leading a group of prisoners of war out of a prison camp. Following his discharge, Mr. A returned to the rural area in which he grew up. He married, worked long hours at his job, and raised three children. He served his community as a volunteer, often distributing food or money to poor families. When he was in his early 60s, after worsening chronic obstructive pulmonary disease and angina, he was forced to retire. He spent much of his time sitting in a chair and could walk only with a cane. Soon after retiring, he began to have recurring nightmares in which he saw heads "popping off" the necks of Korean soldiers. On rare occasions these same images intruded on him during the day. Although he usually slept well, he occasionally awakened with a startle response to noises. One one occasion he assaulted his wife during the night. He began keeping a loaded shotgun next to his bed "just in case." Although he continued to enjoy visiting with friends and family, he stopped visiting the Legion hall because such visits led to increased anxiety. He remained hopeful that his health would eventually improve and allow him to resume his former activities. Although he was frustrated by his disability, he neither complained of nor exhibited cognitive dysfunction or depressed mood. His wife reported that she had never witnessed such symptoms before his retirement and had thought he had put his wartime experiences well behind him.

Although information is limited because of the retrospective nature of the case, Mr. A appears to have been free of psychiatric symptoms for nearly 40 years following exposure to trauma. During those years he worked at an active, physically demanding job and devoted much of his free time to helping those less fortunate. Classic symptoms of PTSD followed his inability to maintain these activities. Detailed interviews uncovered no other potential precipitant of the eruption of symptoms. It is tempting to hypothesize that when his physical condition impaired his ability to function in his usual manner, he was left "defenseless" against the previously invisible underlying psychological distress. Such a hypothesis suggests that the long delay in onset is a reflection of a latent (compensated) rather than an unrecognized disorder. Given the resurgence of interest in dissociative mechanisms active in adaptation to

trauma and breakdown of adaptation (5), the questions raised by this case and others reported in the literature deserve further prospective study.

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Utilization of Inpatient Psychiatric Facilities in Wartime

SIR: The 1991 Persian Gulf war appeared to increase utilization of the 33-bed inpatient psychiatric unit at the Veterans Administration (VA) Medical Center in Syracuse, N.Y. Monthly inpatient census data were reviewed to evaluate this impression. The average occupancy rate in February 1991, the period of the war, was 97%, in contrast to the 82% average February rate of the previous 4 years. These data suggest that the Persian Gulf war had local repercussions, as measured by an increased patient census. We therefore recommend that medical centers, and particularly VA medical centers, consider preparations for increased utilization of inpatient psychiatric facilities in the event of future war.

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Algorithms Versus Decision Trees in *DSM-III-R*

SIR: *DSM-III-R* is incontestably one of the landmark publications in psychiatry. Despite the remarkable care in its preparation, one terminological error appears in appendix B. This appendix presents diagnostic algorithms and not decision trees. This misidentification appears also in the French version of *DSM-III-R*.

An algorithm (1) is a graphic presentation of a sequence of steps to follow, where each step depends on the result of the previous one. A decision tree (2) is a graphic presentation of a sequence of selected options and their issues, including probabilities and utilities of the latter. It represents an overview of alternatives in a way that allows one to find the best decision possible and the one that has greatest probability of a most useful outcome. Hence, an algorithm is a closed system and a decision tree is an open one (3).

A *Dictionary of Epidemiology* (4) gives the following definitions (abridged). An algorithm is any systematic process that

consists of an ordered sequence of steps with each step depending on the outcome of the previous one. A clinical algorithm is an explicit description of steps to be taken in patient care in specified circumstances. A decision tree is a graphic device used in decision analysis, in which series of decision options are represented as branches and subsequent possible outcomes are represented as further branches. The decisions and the eventualities are presented in the order they are likely to occur. The decision tree thus portrays the choices available to those responsible for patient care and the probabilities of each outcome that will follow the choice of a particular action or strategy in patient care. The relative worth of each outcome is preferably also described as a utility or quality of life.

I believe that these concepts should be brought to the attention of readers to allow them to make appropriate corrections and understand properly this important section of *DSM-III-R*.

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Capitalization of Diagnoses in *DSM-IV*

SIR: I have only one suggestion for the editors of *DSM-IV*. It may seem like a trivial matter, but the implications are important. The first letters of the names of psychiatric diagnoses should not be capitalized. *DSM-III-R* does capitalize psychiatric diagnoses, so I am asking that this policy be reviewed and changed.

There appears to be some history of this psychiatric/grammatical phenomenon. In the first *Diagnostic and Statistical Manual of Mental Disorders*, capital letters were not used for diagnoses; for example, "the simple type of schizophrenic reaction characteristically manifests an increase in the severity of symptoms . . . in contrast to the schizoid personality" (p. 26).

In *DSM-II* the style was to begin the first word of a nosological phrase with a capital letter but not the other words. Thus, "this disorder is distinguishable from *Manic-depressive illness* . . . and it is distinguished from *Psychotic depressive reaction* . . ." (p. 36). That style is reminiscent of the method in biology in which the genus begins with a capital letter and the species is lowercase.

Starting with *DSM-III*, the entire phrase was capitalized, with the exception of the prepositions; for example, "however, an Atypical Affective Disorder or Adjustment Disorder with Depressed Mood may be superimposed on Schizophrenia, Residual Type" (p. 187).

What should we do about this creeping capitalization? Does it serve some literary purpose? It would seem to be bad grammar, bad medicine, and bad psychiatry.

1. It certainly does not make sense grammatically to capitalize all of these nouns, which are not proper names. I suppose

the reason was to highlight the official terminology and to make the text easier to understand. That goal can be accomplished by printing the official diagnostic terms in boldface or some other distinctive typeface.

2. Other medical specialties do not begin their diagnoses with capital letters. If you have a broken arm, you simply have a fractured humerus, not a Fractured Humerus. The editors of *DSM-III* and *DSM-III-R* seem to know that. In the illustrations that are given for multiaxial evaluations, the psychiatric diagnoses are capitalized, but the medical diagnoses are lowercase. Is there something that makes Schizophrenia more special than viral encephalitis (*DSM-III*, pp. 30-31)?

3. Capitalizing our diagnostic terms is bad psychiatry because it gives these labels more weight and reality than they deserve. It makes it seem that we are treating some entity called Schizophrenia, Paranoid Type, rather than an individual with paranoid schizophrenia. Other APA publications, such as this journal and *Psychiatric News*, do not capitalize diagnoses, so why does *DSM-III-R*? The problem is that psychiatrists and other mental health professionals read the manual and assume that it is correct to begin these terms with a capital letter.

WILLIAM BERNET, M.D.
Germantown, Tenn.

Alcoholic Mood Syndrome or Major Depressive Disorder With Alcoholism? A Challenge for *DSM-IV*

SIR: We read with interest the article by Allen Frances, M.D., and associates (1) about the development of *DSM-IV*. Among other topics, the authors said that a work group on substance abuse is studying "various ways of defining when psychopathology is best considered secondary to substance intoxication or withdrawal." Such a problem is well illustrated by three very common clinical situations, such as alcoholism, depression, and their overlaps. According to Berglund's meta-analysis (2), 41% of alcoholic patients show simultaneously a depressive syndrome.

When should the clinician consider or not consider the comorbidity in such cases? Theoretically, in *DSM-III-R* the existence of an initiating and maintaining organic factor is an exclusionary criterion for diagnosing major depression. Here the hierarchical model still prevails over the comorbidity. This is consistent with the clinical fact that among alcoholic patients who are "depressed" during their intoxication or at the beginning of withdrawal, many but not all will experience the disappearance of the depressive syndrome within a few days or a few weeks after withdrawal.

However, the vagueness of the exclusionary criterion often leaves the clinician in a state of uncertainty when he or she faces in practice a patient who is apparently both alcoholic and depressive. The chronology of alcoholism versus depression is sometimes difficult to determine. In the case of depression following alcoholism, the causal relationship may not be clear. Indirect arguments can be used, such as a personal or familial history of mood disorder favoring the hypothesis of a current mood disorder. In the Structured Clinical Interview for *DSM-III-R* (3), but not in *DSM-III-R* itself, questions concerning the degree of and possible change in alcoholic consumption are added to try to refine the diagnostic differentiation.

For our particular example, the proposal of Spitzer et al. (4) to rename some "organic" disorders by using the term "secondary" disorders seems, unless it is followed by better-de-

finer or new criteria, to be only a semantic change that does not improve the practical utility and reliability of the classification. From our experience (5), we think that a criterion that well differentiates alcoholic (organic or secondary) mood disorder and primary mood disorder—of which the physiopathology, prognosis, and treatment are radically different—is the persistence or the disappearance of the depressive syndrome after a period of abstinence of approximately 1 month. Such a criterion could be considered for *DSM-IV*.

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L. THERET, M.D.
J.-G. PASCALIS, M.D.
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Dr. Frances and Associates Reply

SIR: Dr. Theret and Dr. Pascalis correctly point out that *DSM-III-R* provides little guidance to the clinician for determining whether a given presenting symptom picture is primary or substance-induced. Indeed, as they suggest, the problem of how best to formulate rules for diagnosing coexisting substance use and other psychopathology is a major challenge to psychiatric nosology. The development of uniform guidelines is further complicated by the large number of classes of substances and the varied symptom presentations associated with them.

Early in its deliberations, the *DSM-IV* work group on substance use disorders identified this issue as an important one for its consideration. An extensive summary of the available literature has been compiled by Dr. Marc Schuckit and reviewed by a large number of advisers to the work group. On the basis of this review, the following two criteria are proposed for inclusion in the sets of criteria describing the substance-induced mental disorders (substance-induced mood disorder is offered as an example).

There is evidence from the history, physical examination, or laboratory findings of substance use, and the symptoms developed during use of the substance or within 6 weeks of the cessation of the substance use.

The disturbance is not better accounted for by a mood disorder that is not substance-induced. Evidence that the symptoms are better accounted for by a mood disorder that is not substance-induced might include: the symptoms precede the onset of the substance abuse or dependence, persist for greater than 6 weeks after the cessation of substance use, or are substantially in excess of what would be expected given the character, duration, or amount of the substance used.

The purpose of these criteria is to advise the clinician to be cautious in making a diagnosis of a mood disorder during the 6-week period following substance use and to allow for clinical judgment in weighing the role of the substance in causing the symptoms. These guidelines, coupled with additional discussion in the text of *DSM-IV*, might provide some help with this often difficult decision.

The proposed criteria for all of the substance-induced disorders are available in the *DSM-IV Options Book* (1). We would appreciate any additional comments and suggestions about how best to deal with this crucially important issue.

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Revising Diagnostic Criteria for Delirium

SIR: Benjamin Liptzin, M.D., and his colleagues presented data in their article “An Empirical Study of Diagnostic Criteria for Delirium” (1) that they believe are useful as a basis for revising the *DSM-III-R* criteria for delirium. However, because of limitations in the design of their study, the “data” raise more questions than they answer.

All of the symptom ratings used for the *DSM-III*, *DSM-III-R*, and *ICD-10* diagnoses of delirium were made by non-clinician research assistants. We are told that they previously demonstrated “good agreement” with the symptom ratings done by a trained neurologist and psychiatrist, yet we are not told how good the agreement was with the actual diagnosis of delirium. This is crucial, since the study never used a consensus or expert clinician diagnosis of delirium. Thus, the reader is never presented with the sensitivity and specificity of the three sets of diagnostic criteria that are being compared.

Especially troubling is the decision to not include the conceptually important *DSM-III* and *DSM-III-R* criterion “clinical features develop over a short period of time (usually hours to days) and tend to fluctuate over the course of a day.” Because a clinical concept is difficult to operationalize (as this criterion is), this is not a sufficient basis for ignoring it. Through the failure to include this criterion, many patients with slowly developing dementia may have been falsely diagnosed as having delirium with the *DSM-III* and *DSM-III-R* criteria sets. Since the study did not include expert clinical rating of delirium, there is no way to know how often this might have happened.

The sample size of 325 patients who were evaluated daily over their entire hospital stay is impressive, but so much more would have been learned about how the diagnostic criteria for delirium could be improved if a smaller number of patients had been studied at one or two points in time by a group of clinicians with special expertise in diagnosing the disorder. This would have provided sensitivity and specificity rates for the criteria sets that were studied, as well as rates for any newly proposed set of criteria.

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ROBERT L. SPITZER, M.D.
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Dr. Liptzin Replies

SIR: I thank Dr. Spitzer for raising some important questions about our study on delirium. The problem with his criticism is that a consensus or expert diagnosis might not have been comparable to any of the official diagnostic criteria. What our study showed was that when the explicit criteria are used, *DSM-III* identifies somewhat more cases than *DSM-III-R* and considerably more than *ICD-10* (research criteria). It is unlikely that patients with slowly developing dementia were falsely diagnosed as having delirium, since most patients developed their symptoms after their admission to the hospital for a medical or surgical illness and after our initial evaluation. A significant number of patients were diagnosed as demented by the treating clinicians, and only those who developed new symptoms in the hospital were also diagnosed as delirious. The basic problem is that until there is some agreed-upon set of criteria for delirium, there will be no way to determine the sensitivity and specificity of any particular screening procedure.

BENJAMIN LIPTZIN, M.D.
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Targeted Neuroleptic Medication

SIR: It has been stimulating to read the contributions of William T. Carpenter, Jr., and his colleagues over the years. Their recent article (1) continues to inform us in the promising but complex area of targeted neuroleptic treatment. However, it appears to me that the most informative study remains to be done.

It first occurred to me in 1979 that a targeted neuroleptic approach was a compellingly sensible alternative, and I have had many opportunities to use it since. My experience is that, using either the patient's developing ability for self-monitoring or that of his or her caretakers (depending on the circumstances), it works well in terms of cognitive, interpersonal, and vocational functioning in some patients (call them group A). However, while it works much better in these patients than continuous neuroleptic treatment does, it yields considerably worse results in others (group B), who cannot or will not use the targeted approach properly.

Furthermore, I find that although several patient-related factors are somewhat predictive, it only really becomes clear which patients can use the targeted approach as one works with them, and it depends on the strength of the therapeutic alliance (in Greenson's sense [2] of the term) with the psychiatrist and the targeted approach itself.

These considerations would have led me to predict that a straightforward comparison of the targeted approach and a constant-dose strategy in unselected patients would yield results confounded by the fact that group A patients do well under one condition and poorly under the other, while group B performs conversely. I suspect this occurred in the study by Carpenter and associates (1).

Finally, there appears to be a group that requires a low continuous dose, with occasional "targeted" increases. This could be characterized as a targeted approach in which the constant dose is as low as possible, a generalization of the approaches of both Carpenter and associates and Lieberman et al. (3).

Putting these considerations together, it seems to me that the clinical trial which would yield the most informative and clinically relevant results would be the comparison of 1) a flexible approach, with medication prescribed as the clinician felt most appropriate (i.e., the targeted approach in the most generalized sense) whenever it seemed promising, and 2) any constant-dosage regimen. The acid test would be one in which the constant dose was individually "optimized" for each patient at the outset of the study period and could be reset periodically but not "targeted."

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PETER GREY, M.D.
Framingham, Mass.

Dr. Carpenter and Associates Reply

SIR: We appreciate Dr. Grey's thoughtful attention to the targeted medication approach. We agree that the results in our study may have been confounded by mixing good and poor candidates in each treatment. As we noted in the article, the experimental trial of unselected cases randomly assigned to treatment may have yielded results that tended to understate any clinical advantage of the targeted approach. Our decision not to preselect candidates for a dosage reduction strategy was based on our original intent to assess the applicability of the targeted approach to a general clinical population of schizophrenic outpatients. One aim, in this regard, was to evaluate empirically the criteria associated with good and poor outcome in each treatment. This evaluation is presently being prepared for publication, but the task of identifying treatment-relevant subgroups in small study cohorts is always difficult.

A better opportunity to identify selection criteria may emerge from the current NIMH five-center treatment study, which contrasts continuous standard-dose neuroleptic medication, continuous low-dose neuroleptic medication, and targeted neuroleptic medication in the context of two separate psychosocial treatment programs. In the meantime, clinicians, such as Dr. Grey, who have developed a thorough knowledge of their patients can more easily and effectively apply the targeted medication approach to these patients than can investigators to their study cohorts. For example, provided they are willing, patients who do not experience severe and frequent relapses would be offered targeted treatment. Those patients who thereafter demonstrated that they could not be maintained without medication for extended periods of time would be placed back on continuous medication. The remaining patients would be the most suitable candidates for long-term continuation of targeted treatment. As Dr. Grey notes, com-

binning the targeted and continuous low-dose medication strategies would also have utility in clinical practice. Dr. Grey's formulation for the "most informative and clinically relevant" study of targeted medication has promise. However, clinical trials comparing two general therapeutic strategies with maximum clinical flexibility often result in a blurred distinction between strategies, thereby requiring exceptionally large sample sizes to detect anything but the most robust differences.

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Modifying the Wisconsin Card Sorting Test Performance of Schizophrenic Patients

SIR: We read with interest the article by Alan S. Bellack, Ph.D., and associates (1), which convincingly demonstrated that schizophrenic patients are capable of improving their performance on the Wisconsin Card Sorting Test after cuing and that performance change does not depend on motivational factors. The positive findings of these researchers stand in contrast to the initial study conducted by Goldberg et al. (2), which concluded that schizophrenic patients have dense impairment in prefrontal functions and fail to maintain any effect of cuing despite explicit card-by-card instruction. We recently completed a study investigating the use of instructional cuing with the Wisconsin Card Sorting Test and several other cognitive measures in schizophrenic subjects (N=24) and comparison subjects with affective disorders (N=24). Our findings may help to clarify those obtained by Dr. Bellack and associates and the related Goldberg et al. study.

Dr. Bellack and associates did not begin their intervention strategy until the schizophrenic patients had completed a block of trials on the Wisconsin Card Sorting Test without cuing, as was the case in the earlier Goldberg et al. study. On the basis of previous work (3) demonstrating that schizophrenic subjects manifest perseverative response tendencies (failure to shift cognitive set despite feedback) early in the course of performance on the test, we chose to target our intervention at the outset of the task. We hypothesized that early intervention would provide an organizational structure and prevent consolidation of perseverative tendencies in the schizophrenic subjects. We used instructional cues similar to those in the Goldberg et al. study but less extensive than those of Dr. Bellack and associates. Our findings revealed significantly less perseveration throughout the test in the cued schizophrenic patients and, to a lesser extent, in the affective disorder subjects than in the noncued patient groups ($F=15.61$, $df=1, 44$, $p<0.001$). The early cuing strategy was performed on other measures (memory function, spatial ability, sequencing), and the schizophrenic subjects demonstrated enhanced performance in these other areas as well.

Among the explanations offered by Dr. Bellack and associates for the disparity between the results of their study and that of Goldberg et al. were differences in chronicity of illness and the use of supplemental training. Our study also supports chronicity and supplemental training as valid determinants in the potential for cognitive improvement among schizophrenic patients. Further, we suggest that deficits in organizational structure in schizophrenic patients (possibly frontally mediated)

ated) may underlie performance across a wide variety of cognitive measures, and that early task intervention strategies are particularly salient in facilitating nearly normal cognitive performance in these patients.

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LAUREN TOMPKINS, PH.D.
ROBERT S. GOLDMAN, PH.D.
BRADLEY N. AXELROD, PH.D.
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Dr. Bellack and Associates Reply

SIR: We were pleased to read that Dr. Tompkins and associates were able to reduce perseverative errors made by schizophrenic patients on the Wisconsin Card Sorting Test. Counting our own study, this is the fifth controlled trial we have seen on this topic. Goldberg et al., of course, found no durable effects for brief instructions. M.F. Green et al. (manuscript submitted for publication, 1991) found modest carryover, but there was a marked decline in performance after prompting was discontinued, despite the use of money as a reinforcer. Summerfelt et al. (1) were able to achieve somewhat greater durability with contingent financial incentives. We used a skills training paradigm and also achieved moderate stability.

This series of studies provides a mixed picture of our ability to enhance reasoning and problem-solving skills in schizophrenic patients. In light of the ensuing studies, the original Goldberg et al. report seems overly pessimistic about the possibilities for cognitive rehabilitation. However, all five studies are limited in that they targeted performance on the Wisconsin Card Sorting Test rather than any underlying information-processing impairment or community functioning. The data show that the test does not reflect an irremediable cognitive dysfunction, but they do not permit any firm conclusions about cognitive function per se. Taken together, the five studies could indicate either that the (purported) underlying impairment is remediable or that performance on the Wisconsin Card Sorting Test is determined by multiple cognitive and behavioral factors, at least some of which can be impacted by treatment.

Of course, the test is not of great interest in and of itself. The more significant question still pertains to the nature and plasticity of any underlying structural/functional impairment. In that regard, Dr. Tompkins and associates mention in passing that they were also able to enhance several other measures of information processing, including memory, spatial ability, and sequencing. Such a finding would have considerable importance if it were demonstrated to be generalizable beyond the specific tests targeted for training. We look forward to seeing the full report of their study. In the interim, we would advocate a shift in focus from the Wisconsin Card Sorting Test to measures that are less confounded by interest and attention and that better reflect problem solving in the community.

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KENNETH PODELL, M.A.
Philadelphia, Pa.

Defensiveness and Lifetime Prevalence of Psychiatric Disorder

SIR: An article by Richard D. Lane, M.D., and associates (1) describing the inverse relationship between defensiveness and lifetime prevalence of psychiatric disorder bears some interesting speculations.

First, it would seem necessary to differentiate between the mood disorders on one hand and the psychotic and personality disorders on the other hand. The former category of patients seem particularly likely to be aware of their inner emotional life as well as the outside objective world, while the latter use particular pathological defenses, including denial, to avoid painful reality. One would intuitively suggest, therefore, that a survey for mood disorders would yield differences in lifetime prevalences of these disorders based on the degree of defensiveness of the subjects studied. However, this would not necessarily be so for other psychiatric disorders.

Second, the philosophical implications of these findings, particularly as they relate to the stigma placed on the depressed patient, should not be lost on us. Specifically, the depressed patient in our society is viewed as weaker, less able to cope, and a less valuable member of the community. Perhaps the results of this study should serve to emphasize to all of us that the depressed patient's perceptions of the outside world may indeed be more accurate than those of the average person, who tends to deny more of what he or she sees. Therefore, more attention should be paid to a depressed patient's perceptions of the outside world as models for structuring and improving society at large as well as the community and family from which the depressed person comes.

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DAVID I. MAYERHOFF, M.D.
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Irritable Bowel Syndrome in Patients With Panic Disorder

SIR: We read with great interest the article by Edward A. Walker, M.D., and associates (1) regarding the potential relation between anxiety and irritable bowel syndrome. Our group noted a possible association between panic disorder and irritable bowel syndrome in the course of our work with panic disorder patients, which was the subject of a report several years ago (2). Because of the potential diagnostic overlap between panic disorder and irritable bowel syndrome, we have assessed the prevalence of various psychiatric disorders in patients with irritable bowel syndrome. The preliminary report

(3) on the first 30 subjects studied indicates that panic disorder was present in 23% of patients with irritable bowel syndrome.

We would now like to report our recent finding from a survey of 78 patients diagnosed as having *DSM-III-R* panic disorder with or without agoraphobia. We found that 33 (42%) of 78 patients met the criteria of Thompson et al. (4) for irritable bowel syndrome. While not all of these patients had received the formal diagnosis of irritable bowel syndrome, the majority had been treated by physicians for their gastrointestinal complaints. These data suggest that substantial overlap of patients with irritable bowel syndrome and panic disorder may exist and that further research at the interface may be fruitful.

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Issues in the 1990 Presidential Address

SIR: In his "Presidential Address: Defending Humanistic Values" (1), Herbert Pardes, M.D., correctly stated that the problem with the animal rights movement is that its activist leaders regard human life and health as no more important than animal life. Curiously, a few paragraphs before this, he conveyed indignation at attempts to prevent human abortion and human fetal research.

I would like to suggest that the best way to help animal activist leaders distinguish the importance of human life vis-à-vis animal life would be to emphasize the inviolable dignity of human life at all stages of development through the abolition of abortion and the consequent "harvest" of human fetal tissue for research.

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THOMAS K. NELSON, M.D.
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SIR: I found Dr. Pardes's presidential address surprising. As psychiatrists, we are accustomed, I would assume, to the complexities of life and not given to seeing things in black and white, them and us, which is illustrated in his portrayal of animal activists as irrational antihumanists with no regard for worthy aims such as finding cures for cancer, schizophrenia, etc. That any movement might have extremist elements should not be surprising to him, and his willingness to protect the "publish or perish" ethic, which we know results in animal

abuse under the guise of saving mankind from cancer, is not the kind of thinking that should qualify as a presidential address.

DOUGLAS P. ROBINSON, M.D.
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Co-occurrence of Deafness and Infantile Autism

SIR: Edward R. Ritvo, M.D., and associates (1) reported the co-occurrence of autism with rare diseases, concluding that these cause CNS pathology and then autism. However, their findings are far more consistent with an undiscussed mechanism, namely, that these diseases or syndromes include subtle peripheral ear disorders that occasionally cause autism. This again illustrates the lack of interest of psychiatrists in the development of deaf infants (2).

The fact that one-third of the concurrent diseases that these authors found in autistic children are not known to produce CNS pathology should immediately suggest that brain damage is not the mediator of autism. On the other hand, many of the diseases associated with autism that they list are well-known to cause or be disproportionately associated with congenital inner and/or middle ear deafness irrespective of whether CNS damage also occurs. These include rubella, cytomegalovirus, meningitis, Down's syndrome and other chromosome abnormalities, mucopolysaccharidoses, juvenile diabetes, hypothyroidism, any (all?) cranial dysostoses, retinitis pigmentosa, measles, lues, mumps, and adrenoleukodystrophy.

The incidence of deafness in the authors' table 1 was implausibly low, indicating underascertainment. To give just two bits of supportive evidence, Taylor et al. (3) found a high prevalence of deafness in autism even without associated neurological disorders; deafness of various types occurred in at least 92% of those with congenital rubella syndrome when adequately followed up (4). All subjects diagnosed as (N=23) or suspected to be (N=14) deaf at age 18 months were definitely deaf later on, including four with autism.

Let us, however, for the sake of argument, assume that all deafness in the authors' autistic subjects was correctly reported. Although I have argued elsewhere (5) that otitis media occurs with autism and is a valuable marker of peripheral pathology, I will also ignore the six cases where otitis was specifically mentioned, since it is common in nonautistic children and was obviously underreported. This leaves three autistic children with deafness (one severe, with herpes; one recessive; one bilateral, profound). Given a prevalence of congenital deafness of one in 2,000 and of autism of four in 10,000, the odds of co-occurrence of autism and deafness are one in 5 million. Clearly, autism and deafness were strongly linked. Plantade and Girardin (2) saw six combined cases, including one with congenital rubella and one postmeningitic. Incidentally, meningitis can cause both deafness and CNS damage, but through independent mechanisms. I have already summarized many other lines of evidence supporting peripheral aural pathology in autism (5). In addition, many brainstem evoked response studies show a very high prevalence of deafness; for example, Taylor et al. (3) found various unsuspected peripheral hearing defects in half of their autistic sample.

The brain does not develop properly unless it receives consistent peripheral input at the right time. Instead of groping inside the brain looking for a needle in a haystack, researchers should be examining the barn door.

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Psychotic Patients' Interpretation of Neuroleptic Side Effects

SIR: We read with interest the case report by Susan Vaughan, M.D., and associates (1) on the development of a delusion of external control resulting from neuroleptic-induced akathisia. Akathisia can be difficult to diagnose at times and difficult to distinguish from psychotic agitation or anxiety (2). This is especially true if an otherwise psychotic patient describes subjective experiences of akathisia in terms of being controlled by an outside force (3). The point is not merely academic but is of practical importance. If the akathisia is mistaken as psychosis, then the clinician may be tempted to increase the dose of neuroleptic and actually worsen the condition. This not only causes the patient to suffer more but could ultimately threaten compliance with the medication regimen.

In a recently completed review of prophylactic antiparkinsonian drug use (3), we noted reports in several studies of patients with psychotic complaints related to or incorporating aspects of extrapyramidal side effects (4, 5). Baker et al. (4) reported a patient who incorporated his physical symptoms into his delusional system, stating that a disc jockey in a nearby town was using radio waves to cause his rigidity, oculogyric crisis, and tachycardia. Manos et al. (5) reported a range of psychotic flare-ups, including delusions and hallucinations related to rigidity, akathisia, and akinesia. Patients made such statements as "A woman tried to strangle me last night," "I burn inside," and "A pair of pliers squeezed my body and throat." The authors stressed that the symptoms were "not related to the previous psychotic picture but were the subjective experience or objective manifestations of disturbing extrapyramidal symptomatology" (5). Of interest is the fact that the development of extrapyramidal symptoms and psychiatric deterioration occurred after withdrawal of the antiparkinsonian agents.

It is likely that these episodes occur more frequently than is usually recognized. While it is difficult to predict which patients may develop akathisia, an approach to treatment that aims to limit neuroleptic side effects seems most reasonable. We view the report by Dr. Vaughan and associates as an additional reason to use prophylactic antiparkinsonian agents. They were able eventually to treat the patients without altering the antipsychotic dose. Not only can these agents help to reduce the need to make difficult differential diagnoses, but they may also prevent cases in which neuroleptic side effects are incorporated into the psychotic state.

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Safer Use of MAOIs With Nifedipine to Counteract Potential Hypertensive Crisis

SIR: We greatly appreciate the comments by Morton Fier, M.D. (1) on the use of sublingual nifedipine to treat the hypertensive crisis induced by treatment with monoamine oxidase inhibitors (MAOIs). The sublingual route is documented in a variety of papers (2-4). After reviewing the literature, Houston (4) argued that nifedipine appears to produce a consistent and prompt fall in arterial pressure after a single dose, irrespective of the route of administration (oral, sublingual, buccal, or rectal). However, van Harten et al. (5) demonstrated that absorption of nifedipine after biting a capsule without swallowing its contents was slow and led to a very low plasma level (median=10 ng/ml). If the capsule (10 mg) was bitten and its contents were swallowed, absorption was faster, and a higher plasma level was achieved (82 ng/ml).

Van Harten et al. argued that the positive results obtained by the sublingual application are probably due to swallowing nifedipine. They recommended biting a capsule and swallowing its contents with water, thereby increasing the predictability of the therapeutic response.

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Impact of Insurance Review Process on Inpatient Care

SIR: Glen O. Gabbard, M.D., and associates (1) provided a much-needed perspective by illustrating the psychodynamic

impact that the insurance review process can exert on inpatient care. Their emphasis was on the ways in which insurance review can become incorporated into individual and systems psychopathology. It seems equally plausible, however, that the review process could exert a positive therapeutic influence if handled properly. A comprehensive treatment of the issue might include an additional case example such as the following.

Ms. A was a 22-year-old woman who was admitted to a psychiatric unit with suicidal ideation. Her diagnosis was borderline personality disorder. The inpatient staff noted a disagreement between her outpatient therapist, who believed that Ms. A needed a holding environment and encouragement to uncover traumatic memories, and her outpatient caseworker, who believed that this would promote regression and that a brief hospital stay for crisis intervention only was appropriate. Ms. A appeared to be using this disagreement in the service of defensive splitting, externalizing a conflict over whether she was worthy of being nurtured.

The staff's initial efforts to point out the split failed, with discussions revolving around whether Ms. A was "really" suicidal or "attention seeking and manipulative" or about who was "right," the therapist or the caseworker. The insurance reviewer began pressuring the treatment team to crystallize and justify a plan with defined goals. The reviewer then became the "bad" party who was seen by the patient and some staff members as thwarting the patient's needs.

Finally, a treatment planning meeting was held that included Ms. A, her caseworker, and the inpatient team (the therapist canceled attendance but was advised of the discussion). Staff members explained in a neutral manner the mechanics of insurance review and framed the need to agree on a plan as a problem of limited resources requiring collaborative effort. Ms. A appeared noticeably relieved and productively energized; she provided sensible suggestions based on her knowledge of past hospitalizations. Consensus was reached on a plan, and the episode was productively discussed in the patient's individual psychotherapy.

This case illustrates the potential for insurance review to catalyze reality-based discussion of how to share limited resources for patients who may experience a sense of infinite need. The external pressure may serve to counteract patients' and caregivers' unrealistic sense of timelessness. It may also help to foster collaborative effort in cases of splitting, particularly of the type described by Gordon and Beresin (2) in which caregivers disagree about the fundamental treatment model for inpatient management of borderline personality disorder.

Insurance review can have a therapeutic impact even without the reviewer's active collaboration, but such collaboration may maximize the likelihood of a therapeutic outcome.

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Genetic and Environmental Factors in Psychiatric Disorders

SIR: The article on genetics and psychiatry by David Reiss, M.D., and associates (1) was a welcome counter to the contemporary prejudice that the various psychiatric disorders will be found to be caused by specific genetic defects, which will enable classification according to the involved gene and lead to molecular genetic therapies. They decry the neglect of environmental and, particularly, familial references in recent articles by influential psychiatrists. In agreement with the purpose and tenor of the article, I simply wish to add evidence for their orientation.

The studies carried out by Tienari et al. (2) of the adopted-away offspring of schizophrenic parents, in which the adopting families were studied, are pertinent to Dr. Reiss and associates' thesis. In brief, only 11 (8%) of the 138 index adoptees became schizophrenic. Of these, none was raised in the 55 reasonably healthy adoptive families, whereas eight were raised in 17 of the 35 severely disturbed adoptive families and three in neurotic families. Among the control subjects, two of the 175 became schizophrenic; both were raised in severely disturbed families. The study provides evidence of a genetic influence, although it seems effective only when the rearing environment is seriously disturbed, but not decisively so; only half of those raised in disturbed families became schizophrenic. The results suggest the possibility or even the likelihood that rather than the genetic factor being specific, the family transactions may be specific, as indicated long ago by the investigations of Lidz and associates, Wynne and associates, Bateson and Jackson, Searles, and Laing.

In their search for studies of "nonshared" environmental influences on siblings that may serve to differentiate genetic from environmental influences, Dr. Reiss and his colleagues overlooked the intensive and prolonged Yale studies of the families of schizophrenic patients, which included only families in which the patient had at least one sibling. My colleagues and I published a rather detailed study (3) of the intrafamilial circumstances that at least contributed to a sibling becoming schizophrenic, seriously disturbed, or reasonably normal and how they differed or resembled the intrafamilial transactions affecting the patient. We only studied the 24 siblings of 16 patients, since a proper differentiation of the very involved influences required intensive and careful study. The various differentiating factors helped clarify the intrafamilial issues that contribute to the production of a schizophrenic offspring. Our findings have been reported sufficiently and will not be repeated here.

I doubt that the careful study necessary to differentiate such familial and other environmental influences can be carried out on 719 families, as Dr. Reiss and his colleagues are attempting to do. The paper on the siblings was republished in the revised edition of *Schizophrenia and the Family*, (4), in which it is followed by the republication of an article on the differentiation of the influences on a pair of monozygotic twins, one of whom became schizophrenic (5), and then of an article concerned with how a set of dizygotic twins raised as monozygotic twins developed intertwined schizophrenic psychoses (6).

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Comments on Self-Injurious Behavior

SIR: The timely review of self-injurious behavior by Ronald M. Winchel, M.D., and Michael Stanley, Ph.D. (1) underscores our fledgling understanding of this phenomenon and raises important questions regarding the neuropsychiatric substrates that may predispose an individual to self-injury. Although the authors addressed many important concepts surrounding self-injurious behavior, we are concerned that, in their proposed definition of the behavior, they use the word "deliberate," implying a conscious or willful act which may not often be evident.

In our experience with the severely and profoundly retarded population at a large developmental center, discerning a motive for repetitive self-injurious acts is very difficult if not impossible. We have been impressed with the apparent compulsiveness of the behavior; in fact, in many cases individuals will seek out restraining devices and become visibly anxious when restraints are removed. Perhaps the insertion of a qualifying statement, "seemingly deliberate," would capture what the authors meant to describe.

Another concern deals with the authors' statements 1) that self-injurious behavior among individuals with mental retardation of etiologies other than the Lesch-Nyhan and Cornelia de Lange syndromes is less severe and less refractory to behavioral management and 2) that self-injurious behavior in these individuals (nonsyndromal) usually appears only after institutionalization.

Regarding the first issue, the authors must know that these two syndromes are extraordinarily rare and make up an insignificant fraction of the total population of mentally retarded persons with self-injury. Indeed, at the Lanterman Developmental Center in Pomona, Calif., there is not a single case of Lesch-Nyhan syndrome among the more than 1,100 mentally retarded residents. On the other hand, self-injurious behavior is present in 25%-40% of individuals residing in California developmental centers overall (2) and occurs on a daily basis in over 100 of those at the Lanterman center. Self-biting can be a dramatic symptom. But self-biting does not occur exclusively in the Lesch-Nyhan or Cornelia de Lange syndromes, nor is there uniformity with regard to the severity of self-injurious behavior within these disorders.

In regard to the second issue, to our knowledge there is no evidence to support the inference that institutionalization of retarded individuals causes self-injurious behavior. In fact, the presence of unremitting or unmanageable behavior of this kind is often among the precipitants for institutionalization.

In sum, we believe it important to underscore that self-in-

jurious behavior is not a diagnosis but a symptom. Self-injury is unique to neither a specific disorder nor a single environment. Just as with the psychiatric population in general, the approach to the mentally retarded patient must be individualized.

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Dr. Winchel and Dr. Stanley Reply

SIR: Dr. King and Dr. Poland point out that self-injury among mentally retarded individuals should not necessarily be described as deliberate. Certainly, the act of self-injury may often occur as a result of a powerful compulsion that the individual might prefer to resist but cannot. As such, the individual does not "want" to hurt himself. While a conscious motive to self-injure is absent in such circumstances, nevertheless the self-injuring behavior is purposeful. We regard this distinction as important because it focuses attention on the rewarding quality of the self-injuring act. The scientific understanding of the rewarding quality of such behavior is still obscure, but in order to address this question, we must acknowledge that the injury is not merely an epiphenomenon but the endpoint of the behavior in question.

In regard to our discussion of the Lesch-Nyhan and Cornelia de Lange syndromes, we certainly clarified in our article the rarity of these syndromes. As we noted, their prominence in our discussion was based on the potential utility of these conditions as models for self-injuring behavior. In contrast with other conditions associated with self-injury, the Lesch-Nyhan syndrome has been the basis for several attempts to produce laboratory models of self-injuring behavior. These studies were described in our article.

Finally, Dr. King and Dr. Poland question the proposition that confinement facilitates the expression of self-injury. We did not state that institutionalization causes self-injurious behavior, nor would we suggest that it does. Inference of a statement of causality is a misunderstanding of our article. However, our review of the literature revealed an abundance of references to the first appearance of self-injury after institutional confinement in both mentally retarded and nonretarded populations. If there is a connection between confinement and self-injury, it most likely would reflect a potentiation of a self-injuring diathesis. (In other words, individuals may differ in their risk for self-injury. Those at risk may express this behavior most frequently under facilitating conditions. For example, Virkkunen [1] found notable differences between prisoners who did and did not self-injure.) Certainly, there is no available research that proves or disproves this hypothesis. But defining such potentiating conditions, as well as defining behavioral and biological markers of those at risk, may teach us much about how to diminish such behavior and may provide insight, as well, into the neurobehavioral bases of self-injury.

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Laws on Reporting Sexual Abuse of Children

SIR: Fred S. Berlin, M.D., Ph.D., and associates (1) reported a steep drop in the number of disclosures of relapse by their pedophilia patients over a 2-year period and attributed the sudden change to less restrictive mandatory reporting laws in Maryland. The number of patients disclosing relapse ranged from 12 (in 1984) to 20 (projected for 1988) and then dropped to absolute zero for all years since the legislative changes. Dr. Berlin and colleagues concluded that the statutory changes were counterproductive in the detection of abuse and in protection of children. I would like to suggest that this, and their other conclusions, have questionable validity and utility on a number of grounds.

First, Maryland laws changed from requiring a report of *observing* a child suspected of being abused to required *reporting* of suspected abuse. Contrary to the experience of Dr. Berlin and associates, research has demonstrated that laws similar to Maryland's new statute increase clinicians' reporting when a third party discloses abuse (2, and manuscript by S.C. Kalichman and C.L. Brosig, submitted for publication). Second, there was increased reporting of sexual child abuse in Maryland over the same time period that there was a decrease in reporting in Dr. Berlin and associates' clinic. Reported sexual abuse increased 5% from 1987 to 1988 and 7% from 1988 to 1989 and stabilized at a 1% increase for 1989 to 1990. Thus, counter to the authors' conclusions, the changes in statutory requirements did not reduce reporting. Third, the population served at the clinic they described is not representative of that in most treatment settings in which disclosures of abuse occur. Dr. Berlin and associates indicated that 55% of their clinic's patients are pedophilic, suggesting long-term involvement with psychiatric care and, most likely, the criminal justice system. It is therefore likely that these patients are sensitized to legal problems and would easily be swayed not to disclose relapse. Finally, while it would be unethical not to provide a patient with information needed for informed consent, the procedures used at the clinic described by Dr. Berlin and colleagues may be biased to act as a warning for their patients not to provide information that would require reporting. The concern is that treatment appears to continue in the absence of direct disclosure, implying that relapse, although not discussed, did occur. In a population where relapse is reoffending, avoiding the criminal justice system may increase potential harm to children. Thus, in this case it does not seem to be the law that interfered with child protection but, rather, the policy of the treatment center as it interacted with the law.

A more general concern with this article is that it may detract from a larger problem that clinicians face with respect to laws on reporting child abuse, namely, the ambiguity of statutory requirements. In contrast to Dr. Berlin and associates, the major concern of laws on reporting has been the protection of child victims rather than patients' rights (2-4). While these authors presented a problem faced by their particular treatment setting, it seems that the uniqueness of the population served and the clinic policies do not justify legislative change

to more restrictive reporting laws. Instead, research suggests that legal definitions of abuse should be operationalized and reporting requirements clarified. With more than 4,000 cases of sexual abuse reported in 1990 in Maryland, I hope that policy makers will not be distracted from the larger problems with mandatory reporting laws by the idiosyncratic problems of a single clinic.

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Dr. Berlin and Associates Reply

SIR: Dr. Kalichman challenges our conclusions; however, the article did not contend that mandatory reporting is never useful. It documented that mandatory reporting can deter undetected abusers from coming forward (Dr. Kalichman ignores this finding) and can deter honest self-disclosure during treatment. It concluded that this can result in some children remaining unnecessarily at risk and that, therefore, options to reporting should be available. In some states, such as Pennsylvania, an adult's self-disclosures to a therapist need not be reported (1).

Dr. Kalichman quotes figures showing increased reporting. The more relevant question is whether mandatory reporting statutes increase the number of abused children identified, or even help identify any at all, when adults have been given appropriate information about informed consent. He presents no data on this. Rather, he questions the clinic's informed consent policy. The clinic is honest about the mandate to report. In Michigan, the Court of Appeals ruled that a criminally prosecuted man who had not been given proper information for informed consent about mandatory reporting had been denied due process, overturning his conviction (2).

Dr. Kalichman argues that the population served by our clinic is not representative. It is true that the clinic, unlike many others, often treats adults who potentially could pose a risk to large numbers of children. Prior to changes in Maryland's mandatory reporting statute, the clinic had successfully brought more than 70 such self-referred individuals into treatment. Legislative changes deterred such self-referrals.

Dr. Kalichman speculates about prior involvements of clinic patients with the criminal justice system. Such involvements did not eliminate self-disclosures until Maryland law changed. Thus, it appeared to be changes in the law and not prior involvement with the criminal justice system that deterred self-reporting.

Dr. Kalichman states that clinic treatment appears to continue in the absence of direct disclosure, suggesting that relapse, though not discussed, still occurs. That is precisely the clinic's fear. In the past, when patients acknowledged relapse openly, early preventive intervention was often possible.

Dr. Kalichman states that in contrast to ourselves, the major concern of reporting laws has been to protect child victims rather than patients' rights. All decent persons are concerned about protecting innocent children. The differences that exist are about how best to do so. It is unclear how deterring abusers from coming forward helps children.

The current mandatory reporting laws are not "the idiosyncratic problems of a single clinic." They are a societal problem. Bound by attorney-client privilege, lawyers who know about unreported abuse cannot refer a client for treatment without having that person self-incriminate. Reporting can be required over the objections of an abused child's parents in cases where neither parent was the abusing party. Weinstock and Weinstock (3) documented a number of instances in which reporting was "detrimental, and not in the best interest of the child." Syndicated columnist Ann Landers recently referred a pedophilic person to a self-help group rather than a psychiatrist (4). She did so because mandatory reporting by therapists "deters those who need help the most from seeking treatment. A self-help group can be of tremendous assistance in filling this gap" (personal communication).

It has been said that for every complex problem there is a simple solution—which is usually wrong. Mandatory reporting, without options, is likely a case in point.

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Disturbed Body Image in Inpatients With Eating Disorders

SIR: I would like to comment on the article "Disturbed Body Image in Patients With Eating Disorders" by R. Lynn Horne, M.D., and associates (1). Although the article presented some interesting findings regarding the high degree of body image disturbance among their patients, I question the implications that the authors drew from their results. It did not surprise me to see that body image distortion is equally high among samples of inpatients with bulimia nervosa and inpatients with anorexia nervosa. However, it seems inappropriate to conclude that a sample of bulimia nervosa inpatients is representative of all bulimia nervosa patients and that the DSM-III-R criteria for bulimia nervosa need to be changed on the basis of these findings.

The authors presented no information about comorbid diagnoses in their clinical groups; it seems unlikely that a sample of inpatients would be without additional axis I and/or axis II diagnoses. The extent to which the authors' sample of inpatients with bulimia nervosa presented with affective and personality disorders might have a significant impact on their degree of body image disturbance. It should be noted that the incidence of affective and personality disorders is very high among bulimia nervosa patients, appearing in 30%-60% of tertiary clinic patients (2-4). However, not all bulimia nervosa

patients have affective and/or personality disorders, and such patients are likely to have fewer body image problems than patients with affective and personality disorders. In at least one study (2), bulimia nervosa patients who showed evidence of affective and personality disorders were just as dissatisfied with their bodies as a sample of anorexic inpatients, while bulimia nervosa patients who showed little evidence of affective and personality disorders were no more dissatisfied with their bodies than a control sample of college women.

It is important for readers to be aware that the characteristics of the sample in the study by Dr. Horne and associates may account for the finding of similarities in body disturbance among clinical subgroups. It is also useful for readers to be aware of the multifactorial nature of bulimia nervosa symptoms (5, 6) and that comorbid diagnoses might influence not only body image difficulties but other aspects of clinical presentation.

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Dr. Horne and Associates Reply

SIR: We appreciate Dr. Tobin's letter and the questions he raises. Information about comorbid diagnoses was not the focus of our article but was, of course, obtained. Major depressive disorder was present in 56.3% of the abstaining anorexic patients, 59.1% of the bulimia nervosa patients, and 69.4% of the patients with both eating disorders. This is quite consistent with the figures cited by Dr. Tobin. The prevalence of dysthymia was 10.4% in the anorexic patients, 4.5% in the bulimic patients, and 19.4% in the patients with both disorders. Alcoholism was present 8.3% of the anorexic patients, 40.9% of the bulimic patients, and 25.0% of the patients with both disorders (significantly greater in bulimic patients than in anorexic patients, $p=0.03$). The prevalence of borderline personality disorder was 2.0% in the anorexic patients, 18.2% in the bulimic patients, and 2.8% in the patients with both disorders (significantly greater in bulimic patients than in anorexic patients and those with both disorders, $p<0.02$).

If body image distortion is examined as a function of comorbid diagnoses, only one diagnosis, major depressive disorder, had a significant effect. The average distortion figure by three-dimensional measurement was 1.24 for the eating disorder patients with major depressive disorder and 1.16 for those without ($p<0.02$). All of these significant differences are accounted for by a single group, the bulimic patients. Their body

image distortion rating was 1.13 for those without major depressive disorder and 1.22 for those with major depressive disorder ($p<0.03$). Distortion in body image was related to lifetime prevalence of major depressive disorder but not to severity of the current depression. There was no significant correlation between average body distortion and either the Beck Depression Inventory score or the Zung Depression Scale score for any eating disorder diagnosis.

Much has been written previously about the relation between depression and bulimia (1, and our article). Our hypothesis is that major depressive disorder does not cause bulimia nervosa patients to have greater distortion of body perception. Our finding that patients with major depressive disorder without eating disorder do not differ from normal college students in body perception (unpublished data) would support this. Instead, we believe that greater body image distortion and presence of major depressive disorder are both predictors of poor long-term outcome. A follow-up study to address this issue is currently underway.

Our report was on perception of body size, not how satisfied with their bodies these patients were, as Dr. Tobin discusses in his letter. We did gather data on body satisfaction, but they were not reported in our article. It is extremely important not to confuse physiological perception and psychological satisfaction.

We agree that it would be inappropriate to conclude that a sample of inpatients with bulimia nervosa is representative of all patients with bulimia nervosa. A study of body perception in outpatients with eating disorders has just been concluded and will be reported soon. We also emphasized the need for replication and extension of all of our findings before any changes in *DSM-III-R* criteria are made.

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Disavowal of Pregnancy: An Adjustment Disorder

SIR: We read with great interest the article by David H. Strauss, M.D., and associates about maladaptive denial of physical illness (1). We agree with their proposed definition of adjustment disorder with maladaptive denial of physical disorder. As a confirmation of and supplement to that report, we should like to present results of our survey (J. Kinzl et al., manuscript submitted for publication, 1991) of 27 female patients with disavowal of pregnancy (the disclosure of pregnancy was made between late second trimester and delivery). Disavowal or denial of pregnancy proved to be an adjustment disorder with adaptive functions for the individual (such as reducing unpleasant affects) but with a significantly higher risk of complications. Because of the denial of being pregnant, usual and necessary preventive checkups during pregnancy were not carried out; risk factors such as nicotine abuse, job stress, and radiation stress continued; and warning signs, particularly premature contractions or premature rupture of the membranes, were wrongly interpreted for a long time. One can suppose that the great number of gestational complica-

tions (four cases of fetal death, higher risk of premature birth) in this group could have been reduced by adequate prenatal supervision.

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Benzodiazepine Withdrawal

SIR: Russell Noyes, Jr., M.D., and associates (1) reported that withdrawal phenomena commonly occur after panic disorder patients stop taking alprazolam or diazepam. What is difficult to understand is that these authors concluded that withdrawal symptoms were more frequent after discontinuation of alprazolam. Their data were based on withdrawal assessments conducted until the subjects had been without medication for at least 2 weeks.

Withdrawal symptoms follow the discontinuation of diazepam for at least 3-4 weeks. Withdrawal seizures have occurred 21 days after discontinuation of diazepam. Dr. Noyes and associates should have conducted withdrawal assessments for at least 3-4 weeks after benzodiazepine abstinence. Final assessments performed at 2 weeks may have made diazepam appear clinically gentler than alprazolam for panic disorder patients. If given extra time, it is possible that diazepam withdrawal phenomena would have bloomed later than those of alprazolam.

I am grateful to Dr. Noyes and his associates for shedding additional light on this very important, frequently overlooked, and often minimized topic of benzodiazepine withdrawal phenomena. I have difficulty understanding the conclusion that these "are more frequent after discontinuation of treatment with shorter-acting drugs" when withdrawal effects of the longer-acting diazepam were not given a chance to blossom.

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JAMES COCORES, M.D.
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Dr. Noyes and Associates Reply

SIR: Dr. Cocores raises an important question about the methods and conclusions of our study comparing the effects of discontinuing short- and long-acting benzodiazepines. He asks why, if withdrawal symptoms following discontinuation of diazepam last for as long as 4 weeks, we did not observe our subjects for a longer time and, given this relatively brief interval, how we were able to conclude that withdrawal phenomena are more frequent after stopping short-acting drugs. Unfortunately, his comments about the time course of withdrawal symptoms are misleading. They imply that symptoms of this kind commonly peak more than 2 weeks after discontinuation of long-acting benzodiazepines. However, a recent study by Rickels et al. (1) showed that the most intense symptoms occurred between 1 and 8 days after abrupt discontinuation of diazepam. Dr. Cocores states that seizures have occurred as long as 21 days after stopping diazepam; however, the median interval for published cases is only 5 days (2). The withdrawal syndrome following abrupt discontinuation of therapeutic doses of long-acting benzodiazepines usually begins in 1-3 days, reaches peak intensity in 3-10 days, and subsides in 2-4 weeks (1-3). The optimal observation period, given this time course, might have been 4 or more weeks after the last dose of drug. However, as in most studies, the design represents a compromise between practical clinical realities and ideal circumstances. In this case we sought to minimize dropouts by reducing the time to completion. Also, because gradual discontinuation tends to shorten the course of any withdrawal syndrome, our observation period extended well beyond the peak intensity for patients discontinuing diazepam. Consequently, we feel that the data from 2 weeks after stopping medication support our conclusion that withdrawal symptoms are more frequent with short-acting drugs.

However, Dr. Cocores's letter calls attention to an important limitation to our conclusions. We observed a similar pattern of rebound anxiety and/or withdrawal symptoms after the discontinuation of alprazolam and diazepam, except that the symptoms appeared sooner and were more severe initially in subjects discontinuing alprazolam. Our data did not allow us to conclude that the overall distress due to alprazolam discontinuation was greater than that from stopping diazepam. The difference may only have been that symptoms developed sooner and were more intense in the beginning. Had we had fewer dropouts and had we observed patients for a longer time, we might have been able to compare overall distress (i.e., Intensity by Duration) resulting from stopping the two drugs. However, we know of no study that has done this or otherwise addressed this important clinical issue. We would like to know whether gradual discontinuation actually reduces withdrawal symptoms or merely extends them over a longer period of time (4), but for the present we do not know which is the case.

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MICHAEL J. GARVEY, M.D.
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MICHAEL SUELZER, M.S.
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Effects of Involuntary Medication

SIR: Concerning the excellent article "Outcome of Involuntary Medication in a State Hospital System" by Francine

Cournos, M.D., and associates (1), I would like to emphasize some points they made that may be overlooked. The authors found in their chronically hospitalized patients that "a course of involuntary medication did not appear to have either a negative or a positive effect on long-term outcome" (p. 492).

One might emphasize that their comparison group included involuntary patients who agreed to medication. I believe it is positive that "forced" medication patients did no worse than comparison subjects. No differences were observed in the amount of restraint or seclusion, despite the fact that more depot neuroleptics were used in the involuntarily medicated patients, as clinicians likely wanted to ensure that these patients with illness of "dire status" (p. 493)—88.2% were dangerous to self or others—received medication. The authors further noted that patients who refuse medication and reach the formal review process may be more severely ill. Therefore, those judged most severely ill and most dangerous did no worse than others. In fact, a significantly larger number of involuntarily medicated patients with documented delusions on admission became less delusional than a group of matched comparison subjects.

Parenthetically, I am reminded that the substance abuse literature reports that outcome of patients' treatment is not related to initial status with respect to seeking treatment: legally coerced or not. "How an individual is exposed to treatment seems to be irrelevant" (2).

Perhaps a better comparison group for Dr. Cournos and associates or others might be the patients themselves, before and after medication, or a group of unmedicated refusers. It is interesting that a group of unmedicated refusers was not possible in the retrospective study by Dr. Cournos and colleagues, as only one of 52 patients' objections to involuntary medication was upheld. This agrees with Schouten and Gutheil's experience in Massachusetts (3), where 99% of petitions are granted over patients' objections per advice of the clinician. This again raises the question of whether judicial reviews are necessary; "due process does not have to mean judicial process" (4). Physicians, not lawyers and judges, should make medical decisions.

The "refusal of antipsychotic medications is associated with major deleterious effects on patient care" (5). Hoge et al. further noted in their prospective study that refusers had higher scores on the Brief Psychiatric Rating Scale, more negative attitudes about all treatment, more negative effects on the hospital milieu, and a higher rate of assaults and threats of assault, were more likely to require seclusion or restraint, and had longer hospitalizations than treatment acceptors (5).

In summary, medication does seem to help in the ongoing treatment of patients clinically judged to need it. Dr. Cournos and associates reinforced the point that medication, whether involuntarily forced or voluntarily taken, may be necessary treatment but is not in itself sufficient treatment over time.

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DANIEL D. STORCH, M.D.
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SIR: In their article, Dr. Cournos and colleagues compared the outcomes of involuntarily medicated patients in a state hospital system with those of voluntarily medicated patients. They concluded that the involuntary medication did not appear to have either a negative or a positive effect on long-term outcomes because the rates of outpatient compliance for both groups, measured 1 year later, were about the same. Since it is well established that patients requiring involuntary medication tend, as a group, to be more psychotic and disorganized and have less insight into their illness and need for treatment (1), this is, in fact, a remarkably positive statement about the utility of involuntary medication in this cohort. Because the involuntarily medicated patients were noncompliant at follow-up at about the same rate as the voluntarily medicated comparison subjects, the authors concluded that involuntary medication "does not produce the insight and cooperation that psychiatrists hope to achieve." Were the authors requiring that involuntarily medicated patients be more compliant than voluntary comparison subjects in order to judge involuntary medication effective? While involuntary treatment is no panacea, several studies have demonstrated that the attitude and behavior of treatment refusers toward accepting medication may change favorably following the episode or course of involuntary treatment (2-4). A long-term rate of compliance for treatment refusers equivalent to that of non-refusers seems to be a very positive outcome, perhaps reflecting such a change in attitude.

The authors' apparent bias against the utility of involuntary medication is reflected in their choice of comparison groups. Comparing the outcome of involuntarily treated patients to that of patients voluntarily receiving treatment misses the central issue which drives the conflict about the right to refuse treatment. Any comparison to the outcome of involuntary treatment should be made with the outcome of failing to treat refusing patients, since involuntary treatment or no treatment at all are the choices faced by the courts, clinicians, and patients when medication is persistently refused.

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HAROLD I. SCHWARTZ, M.D.
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Dr. Cournos and Associates Reply

SIR: We appreciate Dr. Storch's letter. Our own conclusions are that involuntary medication, when used with patients who

have a chronic pattern of treatment refusal and present a danger to themselves or others, is often a necessary and beneficial in-hospital management strategy. However, our study found substantial limitations in the impact of involuntary medication on longer-term outcome. Even with symptom reduction, improvement was often not sufficient for discharge, and half of the study patients remained continuously institutionalized after 1 year. Among those who did leave the hospital, only 30% demonstrated by their actions (attending a clinic and taking medication) that they had come to believe that medication was necessary and worth taking despite side effects.

The hospital is, by its nature, a coercive environment. Although many involuntary patients eventually express agreement with their treatment plans (1), this may not reflect how they will behave on discharge. We hope our report increases awareness of the problems that remain after a course of involuntary medication has been completed.

Dr. Schwartz's letter illustrates the strong emotions provoked by the topic of involuntary medication. Any presentation of data on outcome will elicit, depending on the audience, two contradictory accusations: the researcher is 1) biased against an effective treatment and 2) promoting a harmful treatment that violates the rights of patients.

We attempted to obtain empirical evidence about the impact of involuntary medication in a state hospital system. Our selection of an involuntarily hospitalized comparison group had a clearly stated scientific rationale. The comparison group of unmedicated patients that Dr. Schwartz advocates would be methodologically satisfying but ethically unimaginable. Almost all of our patients were identified as needing medication for reasons of danger to self or others. Under such circumstances, the hospital staff rightly feels compelled to attempt to obtain permission for treatment.

Our results did not show "remarkably positive" effects for involuntarily medicated patients. Psychiatric patients show sufficient improvement when they return to the community and continue treatment of their own volition. That few of our patients achieved this outcome is a fact, not a bias, and this disappoints us as much as it does Dr. Schwartz.

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FRANCINE COURNOIS, M.D.
KAREN MCKINNON, M.A.
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Surreptitious Use of Medication by Placebo Subjects

SIR: In their article on the response of patients with depression to placebo (1), Frederic M. Quitkin, M.D., and associates reported that a substantial proportion of patients improved. In some cases, the improvement persisted. This persistent improvement was interpreted to be the result of spontaneous remission.

In some cases there may be an alternative explanation. My colleagues and I have recently reported that a surprisingly high proportion of panic disorder patients participating in a double-blind, placebo-controlled medication trial were surreptitiously taking antidepressant and anti-anxiety medications (2). While this is a somewhat different population from that re-

ported in the article by Dr. Quitkin and associates, it is quite possible, in my view, that some of the patients in the cited studies were taking prohibited antidepressant medication. As drug screens were not reported, it may not be possible to determine whether this was the case. In future studies using placebo conditions, I recommend that drug screens be performed to detect cases in which the "placebo response" is actually the result of surreptitious use of medication.

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DUNCAN B. CLARK, PH.D., M.D.
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Dr. Quitkin Replies

SIR: Dr. Clark suggests that some of our patients may have surreptitiously been taking nonstudy antidepressants and that this may have accounted for some of the improvement observed in the placebo group. This seems to be an unlikely explanation for the phenomenon observed in this population.

First of all, the overall placebo response rate was low; 25% of the patients taking placebo were judged to be responders after 6 weeks of treatment. This is well within the range of usual placebo response. While we did not measure blood levels in patients taking placebo, 50 patients chosen at random who were taking tricyclics were examined. For these 50 patients, their chromatograms failed to reveal any peaks within the retention time of tricyclics other than imipramine, suggesting that patients in this population did not self-medicate with other antidepressants.

Finally, the fact that abrupt responses of subjects taking placebo and abrupt responses in the first 2 weeks of patients taking drugs had similar characteristics suggests that it is unlikely that antidepressants were responsible for these phenomena.

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Psychological Comorbidity and Length of Stay

SIR: Stephen M. Saravay, M.D., and associates (1) reported recently an association between psychological comorbidity and length of stay in a sample of general hospital patients. However, the effects of depression, anxiety, and organicity measured by psychological tests were weak, accounting for 1.7%, 1.4%, and 2.9%, respectively, of the variance in length of stay. In their introduction the authors mentioned that my colleagues and I failed to demonstrate a relationship between psychological comorbidity and length of stay in a similar prospective study (2). After controlling for medical diagnosis (and, indirectly, the severity of medical illness), we observed that patients with psychological comorbidity remained in the hospital approximately 2 days longer than other patients. Although not statistically significant, the nature of this effect was in the same direction and order of magnitude (i.e., modest) as

that found by Dr. Saravay and associates. Indeed, symptoms of psychological distress were positively correlated ($r=0.20$) with length of stay, a result similar to that of these authors. However, my clinical experience suggests that the effect of psychological comorbidity on length of stay is greater than was observed in these prospective studies. What, then, might account for the difference?

First, prospective studies published to date have not identified comorbidity emerging during the course of hospitalization. It is possible that missing this emergent comorbidity is likely to reduce the size of the relationship between comorbidity and length of stay, a point acknowledged by Dr. Saravay and associates. Second, sampling patients admitted to general medical and surgical floors may underestimate the effect of comorbidity on length of stay that may be found in other inpatient general hospital populations. The mean \pm SD duration of admission in the study by Dr. Saravay and colleagues and in our study was approximately 9 ± 6 days, a brief period with little variation in which to see a strong association between comorbidity and length of stay. Further, the measure of illness severity used by Dr. Saravay and associates only accounted for 4.8% of the variance in length of stay, raising the possibility that administrative and nonclinical factors may be major determinants of duration of admission. (Alternatively, their measure of illness severity may have been inadequate for this clinical setting.)

I suggest that future studies of psychological comorbidity and length of stay identify emergent as well as initial psychological distress/disorder and examine patient populations that have a longer average duration of admission, include more elderly subjects, and require substantial levels of patient cooperation and motivation to achieve discharge. I suspect that data derived in this way will confirm clinical impressions of the added burdens psychological comorbidity places on medically ill individuals, not only in terms of extra days in the hospital.

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PHILIP L.P. MORRIS, M.D., PH.D.
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Dr. Saravay and Colleagues Reply

SIR: We agree with Dr. Morris's comments. The effect of psychological comorbidity on length of hospital stay is just one measure of the more profound impact that psychiatric and psychological factors may have on the course of medical illness. It certainly is important, as Dr. Morris suggests, to distinguish between preexisting psychological and psychiatric morbidity and the comorbidity that emerges during the course of hospitalization. We, along with others, are currently involved in exploring these issues.

Our findings of statistically significant correlations between psychological factors and length of stay were derived from a general hospital population that was not preselected in any way to enhance the likelihood that psychological or psychiatric factors would increase length of stay. The population included patients coming in for routine surgical procedures, for example, where length of hospitalization is often standardized. The fact that we found significant correlations for this population, in view of the numerous procedural, administrative, and other nonclinical influences that have a bearing on the length of hospital stay, is important in establishing the contribution of psychological factors.

It would be expected by the nature of our study design that whatever variances might be found would be relatively modest. Because of this, our findings cannot immediately be translated into a guide for psychiatric intervention. For this purpose, specific populations and/or diagnostic categories at highest risk for extended hospital stay due to psychological and psychiatric factors need to be defined and identified, so that the effect of clinical treatment approaches in reducing length of stay can be tested. We are currently engaged in this endeavor and are optimistic that the results will yield practical benefits to patient care and hospital management.

We hope that the findings of our study will add credence to those of Dr. Morris and associates and the other studies cited in our article and that, taken as a whole, this growing body of work may influence the direction of clinical care and the allocation of funding resources for consultation-liaison services.

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Reprints of letters to the Editor are not available.

Position Statement: Homosexuality and the Immigration and Naturalization Service

This statement was proposed by the Committee on Gay, Lesbian, and Bisexual Issues¹ of the Council on National Affairs. It was approved by the Assembly of District Branches in May 1991 and by the Board of Trustees in June 1991.

The American Psychiatric Association (APA) strongly opposes all public and private discrimination against homosexuals in such areas as employment, housing, public accommodations, licensing, and immigration and naturalization decisions.

Until at least 1990 the U.S. Immigration and Naturalization Service

considered homosexuality to be a mental illness and used this determination as a basis for the discriminatory exclusion of homosexual visitors and immigrants to the United States.

APA successfully opposed the continued inclusion of homosexuality as a mental illness by the Immigration and Naturalization Service. The Association believes that physical illness, mental illness, or sexual orientation per se should not be a basis for immigration or naturalization exclusion.

APA welcomes the changes in Title VI of the Immigration and Naturalization Act of 1990 and will be available to contribute to work intended to ensure that the immigration policies and practices of the United States are consistent with the relevant sections of that act.

¹ The members of the Committee on Gay, Lesbian, and Bisexual Issues at the time the statement was written were Robert P. Cabaj, M.D. (chairperson), Richard A. Isay, M.D., Margery Sved, M.D., Rochelle L. Klinger, M.D., Marshall Forstein, M.D., and Peggy Hanley-Hackenbruck, M.D.

Position Statement on Child Abuse and Neglect by Adults

This statement was proposed by the Committee on Family Violence and Sexual Abuse¹ of the Council on Children, Adolescents, and Their Families. It was approved by the Assembly of District Branches in May 1991 and by the Board of Trustees in June 1991.

Child abuse and neglect is a major public health problem. Although research, cultural, and forensic considerations have resulted in different definitions, the American Psychiatric Association (APA) maintains that child abuse and neglect exists whenever physical pain and injury, sexual exploitation, or psychological harm has been inflicted on a child by any adult; the problem is only magnified when that adult is responsible for the child's protection and nurturance.

The spectrum of abusive and neglectful experiences includes inadequate food, clothing, or shelter; deprivation of adequate emotional attention and support; inadequacy of protective supervision; infliction of physically painful and damaging injuries under the guise of punishment or discipline; denial of adequate education or health care; exposure to sexual overstimulation or exploitation or other sexually abusive experiences; infliction of personally denigrating and humiliating experiences; and isolation from contact or communication with others, especially those who are emotionally important. No child is invulnerable; every child is affected by such experiences.

Extensive clinical experience has demonstrated the destructive effects on both child victims and child witnesses of abuse and neglect. Child maltreatment contributes to the development of lifelong anxieties, disturbance of behavior, depression, suicidal behavior, substance abuse, and severe disturbances in personality formation. These disturbances may include social isolation, withdrawal, and alienation; antisocial, hostile, and destructive character disorders; disruption of the ability to form or to sustain loving, caring relationships with others; development of paraphilias, including child-abusive aberrations; and inability to adequately parent the next generation of children. Sexual abuse is also a risk factor for HIV infection.

APA therefore states the following:

1. The goals of psychiatric intervention must be, first, the protection of children and other family members from maltreatment and, second, the provision of relevant treatments for children and their families with the aim of reversing the psychological and physical sequelae of the maltreatment, improving the quality of parenting, and preserving the family unit whenever possible.

2. Psychiatrists need to be informed of the mandatory reporting requirements of all applicable laws. The reporting of maltreatment to the appropriate agency is the responsibility of any psychiatrist, treating either or both children and adults. Psychiatrists should have access to legal consultation, to APA, and to their district branches when they have questions about reporting responsibilities and procedures.

3. The needs of children for adequate protection from abuse and neglect and for adequate treatment or care in order to recover from the psychic trauma of victimization must supersede the support for the integrity, reintegration, or reunification of children's families.

4. Parental religious convictions should not stand in the way of providing children and adolescents with essential life-saving medical care, including such psychiatric care. Medical child neglect must be considered present if such care for children is refused by the parents.

5. Whenever alleged abuse or neglect of a child is of such magnitude as to warrant legal action, whether in a civil or a criminal court, it should be the obligation of that court to provide both independent advocacy for the child and psychiatric evaluations of the child and the child's primary caretaker(s) in order to guide the court regarding the protection of the child. These psychiatric evaluations should include recommendations to the court regarding the child's participation in legal proceedings; any need for psychiatric treatment for the child, for the perpetrator (parents or parent substitutes) of the child's alleged maltreatment, and for other family members; placement needs of the child; and/or the termination of parental rights.

6. While judicial action is frequently used to protect the victim and other children and to re-empower the traumatized victim, judicial action in all cases should not further abuse and victimize the child.

7. While policies and procedures of courts and child protective agencies provide useful guidelines, the uniqueness of each child and family must be respected. Individualized assessment of each child's needs and individualized prescriptions for treatment and for delivery of supportive and therapeutic services must be designed and implemented to meet the particular needs of each child and each child's family. Treating psychiatrists and agencies receiving reports of child maltreatment must closely coordinate their work. This close coordination, with the permission of families in treatment, should include feedback to the treating psychiatrist regarding investigations, as well as the ongoing collaboration between psychiatrists and child protective service and law enforcement agencies. This collaboration will assure the safety of children and minimize family disruption and the disruption of treatment for victims and their families.

Furthermore, APA recommends the following:

Reporting laws and protective services. APA supports the efforts of public policy makers to protect children through the enactment of child abuse reporting laws and the development of civil child protective services and specialized child abuse and vice units in the criminal justice system. (Such legislation must include provisions for funding adequate individualized and comprehensive psychiatric assessment and treatment for the victimized child and for the child's family, including foster care when needed.)

Training. At a minimum, the curriculum for training regarding child abuse and neglect would facilitate greater awareness of all forms of domestic violence and their frequent coexistence within the same family; delineate the physician's role and responsibility in prevention, detection, reporting, treatment, and consultation to and collaboration with social service, judicial, and police agencies; and stress the individual and family dynamics of domestic violence in the teaching of diagnostic and intervention techniques for child victims, abusive and neglectful adults, and other members of these families.

Research. Research is vital for interrupting the intergenerational cycle of abuse. Such research necessarily includes biogenetic, neurophysiological, cognitive, and emotional sequelae of all aspects of child maltreatment and the effectiveness of intervention programs. (Such research must involve psychiatrists and must be supported by private and public agencies.)

The uniqueness of each child and family must be respected in designing programs for their protection and treatment. Policies and procedures of courts and child protective agencies should include mechanisms for individualized assessment of each child and each family, and supportive and therapeutic services must be tailored to the particular needs defined during these assessments.

¹ The members of the Committee on Family Violence and Sexual Abuse are Sandra Janet Kaplan, M.D. (chairperson), Marion Zucker Goldstein, M.D., Arthur H. Green, M.D., Elaine Carmen, M.D., Herschel D. Rosenzweig, M.D., Matilda Rice, M.D. (Assembly liaison), Mary Lystad, Ph.D., Howard Davidson (consultant), Christine B.L. Adams, M.D., Karen Taylor-Crawford (corresponding member), David Chadwick, M.D. (corresponding member), and Kathryn Jo Kotrla, M.D. (APA/Burroughs Wellcome Fellow).

THE AMERICAN JOURNAL OF PSYCHIATRY

Special Articles

The Genetic Epidemiology of Bulimia Nervosa

Kenneth S. Kendler, M.D., Charles MacLean, Ph.D., Michael Neale, Ph.D.,
Ronald Kessler, Ph.D., Andrew Heath, D.Phil., and Lindon Eaves, D.Sc.

***Objective:** The authors seek to clarify, from both an epidemiologic and genetic perspective, the major risk factors for bulimia nervosa and to understand the relationship between narrowly defined bulimia and bulimia-like syndromes. **Method:** Personal structured psychiatric interviews were conducted with 2,163 female twins from a population-based register. Psychiatric disorders were assessed using DSM-III-R criteria. **Results:** Lifetime prevalence and risk for narrowly defined bulimia were 2.8% and 4.2%, respectively. Including bulimia-like syndromes increased these estimates to 5.7% and 8.0%, respectively. Risk factors for bulimia included 1) birth after 1960, 2) low paternal care, 3) a history of wide weight fluctuation, dieting, or frequent exercise, 4) a slim ideal body image, 5) low self-esteem, 6) an external locus of control, and 7) high levels of neuroticism. Significant comorbidity was found between bulimia and anorexia nervosa, alcoholism, panic disorder, generalized anxiety disorder, phobia, and major depression. Proband-wise concordance for narrowly defined bulimia was 22.9% in monozygotic and 8.7% in dizygotic twins. The best-fitting model indicated that familial aggregation was due solely to genetic factors with a heritability of liability of 55%. A multiple threshold model indicated that narrowly defined bulimia nervosa and bulimia-like syndromes represented different levels of severity on the same continuum of liability. **Conclusions:** The liability to fully syndromal bulimia nervosa, which affects around one in 25 women at some point in their lives, is substantially influenced by both epidemiologic and genetic risk factors. The same factors that influence the risk for narrowly defined bulimia also influence the risk for less severe bulimia-like syndromes.*

(Am J Psychiatry 1991; 148:1627-1637)

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Supported by NIMH grant MH-40828. The Virginia Twin Registry, established and maintained by W. Nance, M.D., Ph.D., and L. Corey, Ph.D., is supported by NIH grants HD-26746 from the National Institute of Child Health and Human Development and NS-25630 from the National Institute of Neurological and Communicative Disorders and Stroke.

E. Walters, M.S., and L. Thacker, M.S., assisted in the data analysis. P. Winter and J. Spence, M.D., assisted in the zygosity diagnoses. Data were collected under the direction of Ms. P. Waring, assisted by Ms. L. Hopkins. B.T. Walsh, M.D., and A.J. Stunkard, M.D., provided comments on an earlier version of this paper.

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Bulimia nervosa, first delineated as a clinical syndrome in 1979 (1), has become a major focus of psychiatric practice and research. However, relatively little is known about its epidemiology; even less is known about the role of familial factors in the etiology of bulimia.

THE EPIDEMIOLOGY OF BULIMIA

Most studies of the epidemiology of bulimia have examined point prevalence on the basis of self-report questionnaires, often in select populations such as college students (2). Averaged across published studies, the frequency of current binge eating in women has been

estimated at 35%, while 8% report self-induced vomiting and 5.8% laxative abuse (2). On the basis of studies using self-report, the point prevalence of bulimia averages 9.0% for the *DSM-III* definition and 2.6% for the *DSM-III-R* definition. Far fewer studies have used face-to-face interviews, and in only two of those was the entire sample interviewed (3, 4). However, in those two studies the samples were limited to normal-weight volunteers (3) or college students (4). The interview-based studies produced lower estimates for the point prevalence of bulimia in women than the questionnaire-based studies: 1.5% using *DSM-III* and 0.9% using *DSM-III-R* criteria (2).

Two studies have recently reported lifetime prevalence rates for *DSM-III* bulimia nervosa. In a general population sample from New Zealand, assessed by lay interviewers, the lifetime prevalence of bulimia in women aged 18–44 was 2.6% (5). However, on the basis of clinician interviews of a subset of this sample, the estimated lifetime prevalence of bulimia in the same sample was lower (1.7%) (5). Using two-stage screening with high school students from New Jersey, Whitaker et al. (6) found that the lifetime prevalence of bulimia was 4.2% in girls. One epidemiologic study of bulimia ascertained subjects through treatment facilities and found, using *DSM-III* criteria, a 2-year prevalence of treated bulimia in females aged 16–24 of 0.4% (7). These results, consistent with those found by others (4, 6, 8, 9), indicate that a minority of subjects with bulimia seek treatment.

Studies of the epidemiology of bulimia frequently note that, in the general population, the syndrome is more a spectrum of pathology than a discrete disease entity (2–5, 8, 10, 11). For example, in a general practice survey in London, patients with “partial-syndrome eating disorder” outnumbered patients with classic cases of bulimia by more than two to one (11). A recent review recommended “a shift in emphasis away from studies of the distribution of the disorder toward studies of the determinants of the whole spectrum of the disturbance that exists in the community” (2).

FAMILY/GENETIC STUDIES OF BULIMIA

While a number of studies have examined the risk of affective illness in relatives of patients with bulimia (12, 13), only four published reports have examined whether bulimia itself aggregates in families. Using *DSM-III* criteria, Hudson et al. (14), in an uncontrolled family history study, found that the prevalence of bulimia in relatives of bulimic probands was 3.4%. In a later controlled family history study, the same group found that the risk for bulimia was 2.2% in relatives of bulimic probands; this prevalence was nonsignificantly higher than the 0% risk in relatives of control subjects (15). Logue et al. (16) found no case of bulimia in interviewed relatives of bulimic probands who were ascertained through treatment facilities. By contrast, Kasset et al. (13), using direct interviews with relatives,

found that the risk for bulimia in relatives of hospitalized bulimic probands was 9.6%, versus 3.5% in relatives of normal control subjects ($p < 0.05$).

Of the four published reports, only one (13) provides robust evidence for the familial aggregation of bulimia. These reports suffer from several methodologic limitations. Risk for bulimia is not reported separately for female and male relatives. Two of the studies relied on family history information only, which may have only modest sensitivity. All reports ascertained probands through psychiatric treatment facilities, which may produce a proband sample that lacks the milder cases of bulimia commonly seen in the community or in primary care settings.

We are aware of two published twin studies of bulimia. Hsu et al. (17) examined 11 twin probands with bulimia who were referred to an eating disorders clinic. The co-twin was personally interviewed in six pairs. Two of the six monozygotic female-female pairs (33%) were concordant for bulimia, compared to none of the five dizygotic pairs (two female-female and three male-female pairs). Fichter and Noegel (18) ascertained 27 twin pairs with bulimia from volunteers to a press survey (17 pairs) and two clinical services (10 pairs). Diagnosis was made using *DSM-III-R* criteria applied to a self-report measure. Excluding the one male monozygotic pair and the five opposite-sex dizygotic pairs, they reported pairwise concordance for bulimia nervosa in five of six female monozygotic pairs (83%) and in four of 15 female dizygotic pairs (27%).

In this report, we examine the epidemiology and genetics of bulimia in 2,163 female twins from a population-based registry in which bulimia and bulimic-like syndromes were assessed by personal interview.

METHOD

Sample

Data for this report come from an ongoing study of genetic and environmental risk factors for common psychiatric disorders in Caucasian female same-sex twin pairs from the Virginia Twin Registry. The Virginia Twin Registry is a population-based register formed from a systematic review of all birth records in the Commonwealth of Virginia. Current addresses are obtained by a variety of means, including matching with state records.

Twins were eligible to participate in this study if both members of the pair had previously responded to a mailed questionnaire, the individual response rate to which was 64%. This is certainly an underestimate of the cooperation rate, as an unknown proportion of the twins did not receive the questionnaire because of lack of correct addresses. In a total of 1,176 twin pairs, both members returned questionnaires and thus were eligible for the personal interview phase of the study. In 46 pairs, neither twin was successfully interviewed. In 97 pairs, one twin was interviewed and the other refused.

In 1,033 pairs, both twins were interviewed. During the personal interview phase of the project, therefore, the individual response rate was 91.8%. Of the completed interviews, 89.3% were performed face to face, usually in the twin's home, and 10.7% (primarily twins residing outside Virginia) were interviewed by telephone. The mean \pm SD age of the sample at interview was 30.1 \pm 7.6 years (range=17-55).

Determination of Zygosity

Information on zygosity for each twin pair in which both members participated in the interview was reviewed by two experienced twin researchers who were blind to all information about the psychiatric status of the twins. This information included the response to questions about physical similarity and frequency of confusion as children (which have been shown to be able to identify zygosity in twins with over 95% accuracy) (19) and, in over 80% of cases, photographs of both twins. Twin pairs were divided into five groups: definitely monozygotic, definitely dizygotic, probably monozygotic, probably dizygotic, and uncertain. Disagreement between the two raters was resolved by consensus. We attempted to obtain blood samples from both members of the pairs in the final three categories and were successful in 119 of the 186 pairs so classified. Zygosity was determined by DNA analysis using eight highly polymorphic probes (20). The probability of monozygosity for twins identical at all eight loci was 0.9997. Final determination of zygosity, which used DNA results when available and otherwise a diagnosis of definite or probable zygosity, yielded 590 monozygotic twin pairs, 440 dizygotic twin pairs, and three pairs classified as uncertain. In 105 twins with a diagnosis of probable zygosity, DNA methods validated our assignment in 87 of the cases (83%). DNA or protein polymorphism zygosity information was available for 26 twins with a diagnosis of definite zygosity and validated our assignment in all cases.

Measures and Interviewers

Lifetime psychiatric illness was diagnosed with an adapted version of the Structured Clinical Interview for DSM-III-R (21). All interviewers, who had at least a master's degree in social work or a bachelor's degree and 2 years of social work or counseling experience, were initially trained for 80 hours and received bi-monthly review sessions over the course of the study, which was completed between September 1987 and July 1989. The same interviewer never interviewed both members of a twin pair.

To assess the similarity of childhood environment, twins were asked how often, as children, they 1) shared the same room, 2) had the same playmates, 3) were dressed alike, and 4) were in the same classes. Answers to these questions were summed to form a single index of childhood similarity. Twins were also asked how frequently they were in current contact with their co-

twins, with response options ranging from "living together" to "once a year or less."

Personality was assessed by the short version of Eysenck's Personality Questionnaire (22), self-esteem by the Rosenberg Self-Esteem scale (23), and locus of control by a modified form of the Attributional Styles Questionnaire (24). Maternal and paternal care and overprotectiveness were assessed by seven items selected from the Parental Bonding Instrument (25).

In part of our sample (N=1,375), the twins returned, 1 to 3 years before interview, a questionnaire providing further information about weight, level of exercise, and body image as assessed by body silhouettes (26). The twins were asked which silhouettes were "closest to the usual appearance" ("usual silhouette") of themselves, their mother, and their father and which silhouette they would "like to look like" ("ideal" silhouette).

Diagnostic Review

Final project diagnoses were based on a blind review of the entire interview by one of us (K.S.K.), an experienced psychiatric diagnostician. Diagnoses were made at three levels of certainty—definite, probable, and possible—using *DSM-III-R* criteria. For a definite diagnosis, all diagnostic criteria had to be met with sufficient severity or certainty that the individual, if seen in a clinical setting, would definitely be considered a "case." A probable diagnosis meant that the diagnostic criteria were met, but the severity or certainty of these symptoms was less impressive. A possible diagnosis was given when most but not all of the diagnostic criteria were met and the syndrome was considered to be clinically significant.

Statistical Analysis

The analysis of epidemiologic risk factors for bulimia nervosa was performed using logistic regression (27) in two different ways (results available on request). First, analyses were conducted treating each twin as a separate observation; the dependent variable was the affection status of the twin. Second, analyses were repeated in which each complete twin pair was a single observation. The independent variables were the mean values of the two members; the dependent variable became ordinal: 0=neither twin affected, 1=one twin affected, and 2=both twins affected. When the dependent variable is modestly correlated in pairs of observations, the former method should be slightly statistically liberal, while the latter method should be quite conservative. These methods differed in assigning significance (at the 5% level) in three of the 25 regression analyses reported here. In two of these, the results were significant only by the presumably more conservative second method. We therefore present results from the first method, which treats the twins as separate observations.

In all regression analyses, age was included as a control variable and the statistical significance of the independent variable was determined by a chi-square test with one degree of freedom. To test the "equal environ-

ment assumption," the impact of childhood similarity or frequency of contact on twin similarity for bulimia was assessed by logistic regression in which the dependent variable coded zero if the twins were concordant (i.e., both or neither twin had a diagnosis of bulimia) or one if they were discordant.

Given that the risk for bulimia is correlated in twins, if bulimic individuals are less likely to cooperate with personal interviews, then the risk for bulimia should be higher in twins whose co-twin was not versus was successfully interviewed. This can be assessed by logistic regression using a dummy independent variable for interview status of co-twin.

Body mass index was calculated as weight divided by height squared. The magnitude of comorbidity in possible versus definite and probable cases of bulimia was compared by examining the difference in odds ratios (28). Lifetime risk was calculated by life table analysis. The statistical test between survival curves was conducted using Cox's proportional hazard model (27).

The analysis of the twin data is based on a "liability-threshold" model which assumes that underlying the observed dichotomous distribution of "unaffected/affected," there exists a continuous, normally distributed latent liability (29). The observed discontinuous distribution is assumed to emerge from the imposition of a threshold on the normally distributed latent liability. This model assumes that the genetic and environmental factors contributing to the liability to bulimia act additively and are relatively numerous and small in magnitude. Although this model classically assumes a large number of genes, a normal distribution of liability can be closely approximated by a quite small number of genes (30).

When the discrete distribution contains only two categories (e.g., unaffected/affected), a correlation in liability (or, more technically, a tetrachoric correlation) is calculated from the 2x2 contingency table of twin 1's and twin 2's affection status. This statistic is superior to the traditional concordance rate calculated in twin studies because it takes into account both concordance for affection *and* concordance for nonaffection.

A tetrachoric correlation fit to a 2x2 table is a "perfect fit" and provides no test of the model. However, in testing whether possible, probable, and definite cases of bulimia can be assumed to represent different levels of severity in the same liability continuum, a polychoric correlation is calculated from the 4x4 table, cross-tabulating the diagnoses of the two twins (unaffected and the three levels of diagnostic certainty). A chi-square goodness of fit test is then available for testing the distributional assumptions made in calculating the polychoric correlation.

The tetra- or polychoric correlations for twin 1 and twin 2 were separately computed for monozygotic and dizygotic twins using the computer program PRELIS (31). Models were fit to these correlations using the computer program LISREL (32-34). The goal of these analyses was to obtain estimates for the proportion of variance in the underlying liability to bulimia that was due to additive genetic factors (A), family or "com-

mon" environment (C; environmental factors shared by both members of a twin pair such as rearing environment, social class, and school), and individual specific environment (E; environmental influences unique to each member of a twin pair, including any unreliability of measurement). We began by fitting an ACE model that included additive genes, family environment, and individual specific environment. The fit of this model was assessed by a goodness of fit chi-square test. We then fitted two simpler models that postulate markedly different causes for any observed familial aggregation of bulimia. The AE model assumes that all familial aggregation results from additive genetic effects, while the CE model assumes that all observed familial aggregation is the result of shared environmental influences. The fit of each of these models was compared, by a likelihood ratio chi-square test with one degree of freedom, with that found for the ACE model. The best-fitting model was chosen using Akaike's information criterion (35), which reflects both the goodness of fit and the parsimony of the competing models.

RESULTS

Lifetime Prevalence, Risk, and Sampling Bias

Of the 2,163 interviewed twins, 32 were diagnosed as having definite, 28 probable, and 63 possible bulimia nervosa. Because of the limited sample size, and because subjects with both definite and probable bulimia met *DSM-III-R* criteria, for most subsequent analyses we divided our affected twins into two categories: definite and probable cases (sometimes termed *narrowly* defined bulimia) and possible cases. We use the term *broadly* defined bulimia to refer to definite, probable, or possible cases of bulimia. The lifetime prevalence (the proportion of individuals who received the diagnosis at any time in their life) for definite and probable and for possible cases of bulimia was 2.8% (95% confidence interval of 2.1%-3.5%), and 2.9% (95% confidence interval of 2.2%-3.6%), respectively. The lifetime risks (the proportion of individuals who would be *expected* to receive the diagnosis if they completed their age at risk, here defined as age 50) for diagnoses of narrowly and broadly defined bulimia were, respectively, 4.2% and 8.0%.

No evidence was found in the twins for sampling bias with respect to bulimia, as the interview status of the co-twin did not significantly predict risk for broadly defined bulimia nervosa ($\chi^2=0.08$, n.s.). Mode of interview (face to face versus telephone) also did not significantly predict risk for a diagnosis of broadly defined bulimia ($\chi^2=2.10$, n.s.).

Method of Preventing Weight Gain

The methods used to prevent weight gain for twins with definite and probable versus possible bulimia are seen in table 1. Although all methods were more common in the twins with definite and probable bulimia

TABLE 1. Methods Used to Prevent Weight Gain by Female Twins With Possible Versus Definite and Probable Bulimia

Method	Possible Cases		Definite and Probable Cases	
	N	% ^{a,b}	N	% ^a
Self-induced vomiting	13	21.7	24	40.0
Laxative use	12	20.0	18	30.0
Strict dieting	14	23.3	25	41.7
Fasting	12	20.0	22	36.7
Exercise	22	36.7	30	50.0

^aTotals more than 100% because some individuals used more than one method.

^bIn three possible cases, subjects did not describe a specific method.

than in those with possible bulimia, the patterns of methods used to prevent weight gain were similar (i.e., exercise was the most common, followed by strict dieting and vomiting). Self-induced vomiting was used to control weight gain in 40% of the twins with definite and probable bulimia and nearly 22% of the twins with possible bulimia. A review of the remaining *DSM-III-R* criteria for bulimia indicated that the greatest difference between the twins with definite and probable versus possible bulimia was in criterion D ("a minimum average of two binge eating episodes a week for at least three months"). While nearly all subjects with definite and probable bulimia endorsed this criterion, only one-third of the subjects with possible bulimia reported binges at least twice a week for 3 months.

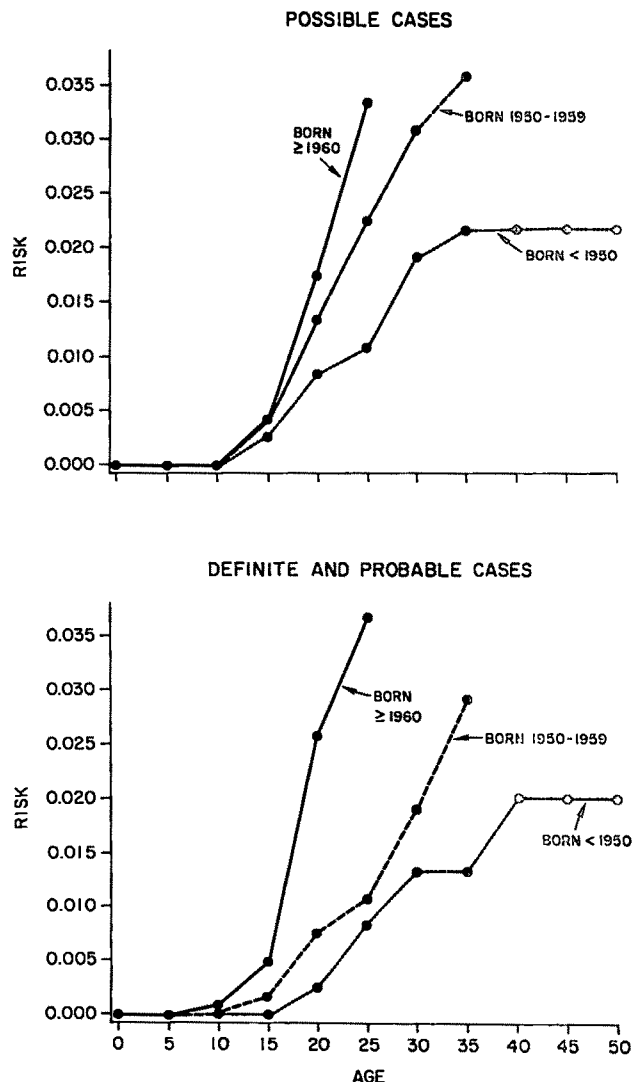
Age at Onset and Cohort Effect

The mean±SD age at onset for subjects with definite and probable bulimia (20.9±6.5 years) was similar to that for the subjects with possible bulimia (20.5±5.3 years) ($t=0.43$, $df=121$, *n.s.*). Current age was negatively, although nonsignificantly, related to lifetime prevalence of bulimia ($\chi^2=1.41$, $df=1$, *n.s.*). This result, which is not explicable by a standard model of cumulative incidence, would be expected if individuals born more recently were at higher risk for the disorder.

To assess the presence of a cohort effect, we divided the sample into twins born before 1950 ($N=367$, mean age at interview=42.3 years), between 1950 and 1959 ($N=761$, mean age=33.0 years), and after 1959 ($N=1,035$, mean age=23.6 years). As seen in figure 1, the survival curves were significantly different across birth cohorts for subjects with both definite and probable bulimia ($\chi^2=14.05$, $df=1$, $p=0.0002$) and possible bulimia ($\chi^2=4.07$, $df=1$, $p=0.04$). The life table curves for definite and probable versus possible bulimia did not significantly differ ($z=1.61$, *n.s.*).

Comorbidity

The 123 subjects with broadly defined bulimia had the following additional lifetime psychiatric disorders: major depression, 63 (51.2%); phobia, 52 (42.3%); alcoholism, 19 (15.5%); generalized anxiety disorder, 14

FIGURE 1. Lifetime Cumulative Risk for Bulimia Among Female Twins Born Before 1950, in 1950–1959, or After 1959^a

^aRisk differed significantly by birth cohorts for both definite and probable bulimia ($\chi^2=14.05$, $df=1$, $p=0.0002$) and possible bulimia ($\chi^2=4.07$, $df=1$, $p=0.04$). However, the pattern of results did not differ significantly between the possible cases and the definite and probable cases (see text).

(11.4%); anorexia nervosa, 12 (9.8%); and panic disorder, 11 (8.9%). Only 28 of the 123 subjects (22.8%) had no other lifetime psychiatric diagnosis.

The odds ratios for psychiatric disorders in subjects with definite and probable versus possible bulimia are seen in table 2. For subjects with definite and probable bulimia, all the odds ratios were statistically significant and ranged from 2.20 for major depression to 8.23 for anorexia nervosa. The pattern of results for subjects with possible bulimia was similar. The magnitude of comorbidity as assessed by the odds ratios did not differ for any of the disorders in the subjects with definite and probable versus possible bulimia.

Because of particular interest in the etiologic relationship between bulimia and depression (36–39), we ex-

TABLE 2. Odds Ratios for Psychiatric Disorders in Female Twins With Definite and Probable Versus Possible Bulimia

DSM-III-R Disorder	Definite and Probable Cases		Possible Cases		χ^2 for Homogeneity
	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	
Major depression	2.20	1.32–3.69	2.44	1.47–4.03	0.08
Phobia	2.37	1.41–3.97	1.65	0.98–2.76	0.95
Generalized anxiety disorder	2.61	1.21–5.62	1.75	0.74–4.14	0.52
Panic	3.00	1.25–7.20	2.30	0.90–5.89	0.17
Alcoholism	3.23	1.55–6.73	3.48	1.72–7.03	0.02
Anorexia nervosa	8.23	3.27–20.70	7.79	3.10–19.54	0.01

TABLE 3. Concordance Rate and Correlations of Liability for Broadly and Narrowly Defined Bulimia in Monozygotic and Dizygotic Female Twins

Diagnosis	Zygosity	Probandwise Concordance		Correlation of Liability
		N	%	
Broad	Monozygotic	18/69	26.1	0.50
Broad	Dizygotic	8/50	16.0	0.31
Narrow	Monozygotic	8/35	22.9	0.55
Narrow	Dizygotic	2/23	8.7	0.27

amined the order of ages at onset of the two disorders in the 63 subjects with both diagnoses. Seven subjects (11.1%) reported onset of both disorders at the same age. Of the remaining 56 subjects, far more reported onset of depression before bulimia ($N=45$) than bulimia before depression ($N=11$) ($\chi^2=20.6$, $df=1$, $p=0.000$). The same pattern of results was seen when only subjects with narrowly defined bulimia were considered.

Social Class, Personality Traits, and Rearing Environment

No significant relationship was found between risk for broadly defined bulimia and social class as indexed by years of education ($\chi^2=1.57$, *n.s.*), income ($\chi^2=0.04$, *n.s.*), or occupation ($\chi^2=2.39$, *n.s.*). Having a college education did not predict risk for bulimia ($\chi^2=0.38$, *n.s.*). Neither parental years of education ($\chi^2=1.40$, *n.s.*) nor parental occupation ($\chi^2=0.74$, *n.s.*) significantly predicted risk for bulimia.

Risk for broadly defined bulimia was unrelated to levels of extraversion ($\chi^2=0.02$, $df=1$, *n.s.*) but was significantly related to high levels of neuroticism ($\chi^2=31.25$, $p<0.0001$), low levels of self-esteem ($\chi^2=26.27$, $p<0.0001$), and an external locus of control ($\chi^2=6.09$, $p=0.01$).

The risk for broadly defined bulimia was unrelated to the level of maternal care ($\chi^2=0.81$, *n.s.*), maternal overprotectiveness ($\chi^2=0.01$, *n.s.*), or paternal overprotectiveness ($\chi^2=0.00$, *n.s.*), but was significantly and negatively related to reported levels of paternal care ($\chi^2=5.32$, $p=0.02$).

Weight, Dieting, Level of Exercise, and Body Image

Current weight ($\chi^2=0.10$, *n.s.*), body mass index ($\chi^2=0.19$, *n.s.*), previous minimum weight since age 18

($\chi^2=0.45$, *n.s.*), and previous maximum weight ($\chi^2=1.12$, *n.s.*) were not significantly related to risk for broadly defined bulimia. However, as assessed on an earlier questionnaire, maximum weight fluctuation (maximum weight–minimum weight) ($\chi^2=8.91$, $p=0.0028$), current dieting ($\chi^2=20.59$, $p<0.0001$), and high levels of exercise ($\chi^2=11.99$, $p=0.0005$) predicted the diagnosis of bulimia made on subsequent interview.

As assessed on this same questionnaire, while the “usual” body image did not predict risk for bulimia ($\chi^2=2.19$, *n.s.*), risk for a subsequent diagnosis of bulimia was associated with a slim ideal body image ($\chi^2=5.26$, $p=0.02$). Neither the usual body image of the mother ($\chi^2=0.95$, *n.s.*) nor that of the father ($\chi^2=0.34$, *n.s.*) significantly predicted risk for bulimia.

Risk Factors for Definite and Probable Versus Possible Bulimia

None of the identified risk factors for broadly defined bulimia significantly discriminated between definite and probable versus possible bulimia. These risk factors included neuroticism ($\chi^2=0.79$, *n.s.*), self-esteem ($\chi^2=0.29$, *n.s.*), locus of control ($\chi^2=1.73$, *n.s.*), low paternal care ($\chi^2=0.22$, *n.s.*), weight fluctuation ($\chi^2=0.01$, *n.s.*), slim ideal body image ($\chi^2=0.35$, *n.s.*), exercise ($\chi^2=1.50$, *n.s.*), and dieting ($\chi^2=0.04$, *n.s.*).

Examination of Potential Biases in Twin Analysis

Zygosity in our sample was unrelated to risk for bulimia ($\chi^2=0.00$, *n.s.*). When age was controlled, monozygotic twins had more similar childhood environments ($\chi^2=15.73$, $p<0.0001$) and more frequent contact with one another as adults ($\chi^2=77.43$, $p<0.0001$) than did dizygotic twins. When the effects of age and zygosity were controlled, however, twin similarity for bulimia was unrelated to either the similarity of childhood environment ($\chi^2=1.08$, *n.s.*) or the frequency of contact as adults ($\chi^2=1.08$, *n.s.*).

Twin Concordance and Correlation of Liability

The probandwise concordance and the correlation in liability for bulimia, broadly and narrowly defined, for monozygotic and dizygotic twins are seen in table 3. When either the broad or narrow definition was used,

TABLE 4. Model Fitting for Broadly and Narrowly Defined Bulimia and the Multiple Threshold Model in Female Twins^a

Definition of Bulimia	ACE ^b	Fit in χ^2 Units			Model	Parameter Estimates		
		CE ^c	AE ^c	E ^d		A	C	E
Broad	0	0.98	0.15 ^e	25.35	Full	0.38	0.13	0.50
					Best fit	0.52	—	0.48
Narrow	0	0.99	0.00 ^e	16.59	Full	0.55	0.00	0.45
					Best fit	0.55	—	0.45
Multiple threshold	0	0.87	0.51 ^e	36.20	Full	0.32	0.22	0.46
					Best fit	0.56	—	0.44

^aA=additive genetic factors, C=family or common environmental factors, E=individual specific environmental factors.

^bdf=0.

^cdf=1.

^ddf=2.

^eBest-fitting model by Akaike's criterion (35).

concordance in both twin types substantially exceeded the population risk, thus providing evidence for the familial aggregation of bulimia. For example, for narrowly defined bulimia, the risk in a monozygotic co-twin of an affected twin exceeded the population risk by over eight times.

When either the broad or narrow definition of illness was used, the concordance rate in monozygotic twins substantially exceeded that found in dizygotic twins (broad definition: 26.1% versus 16.0%; narrow definition: 22.9% versus 8.7%). The correlation in liability for bulimia in monozygotic twins was relatively high (about 0.50 for both definitions) and considerably exceeded that found in dizygotic twins (about 0.30 for both definitions).

Fit of the Multiple Threshold Model

The multiple threshold model provides a statistical test for the hypothesis that possible, probable, and definite cases of bulimia result from the same underlying vulnerability and hence can all be called part of a *bulimia spectrum*. If this model fits well, it supports the hypothesis that subjects with possible, probable, and definite bulimia, in terms of their disease vulnerability, differ quantitatively but not qualitatively. The multiple threshold model fit well in both monozygotic twins (χ^2 goodness of fit=6.80, df=8, $p=0.558$), producing an estimated correlation of liability of 0.54, and in dizygotic twins (χ^2 goodness of fit=10.95, df=8, $p=0.204$), producing an estimated correlation of liability of 0.38.

Twin Model Fitting

The results of model fitting applied to correlations of liability for broadly defined bulimia, narrowly defined bulimia, and bulimia spectrum (obtained with the multiple threshold model) are seen in table 4. The findings, which were similar for all three definitions of illness, can be summarized as follows: 1) the E only model (which predicts no familial resemblance) was strongly rejected; 2) the full ACE model produced estimates of A that exceeded those of C; 3) by Akaike's criterion, the AE model was preferable to the CE model, although the statistical superiority was modest; and 4) the best-fit-

ting model, by Akaike's criterion, produced estimates of the heritability of the liability to bulimia of between 50% and 55%.

DISCUSSION

Prevalence and Risk

Studies using various assessment methods and diagnostic criteria have produced widely varying estimates for the point prevalence of bulimia nervosa in women (2). In studies using personal interviews with *DSM-III-R* criteria, the point prevalence averaged across studies is 0.9% (2). Estimates of lifetime prevalence for *DSM-III* bulimia nervosa in young women have ranged from 1.7% to 4.2% (5, 6). One study, based on clinician re-interviews of a subset of an epidemiologic sample, has estimated lifetime prevalence of *DSM-III-R* bulimia, in women aged 18–44, at 1.6% (5). In the present study, the first to our knowledge to assess lifetime prevalence using *DSM-III-R* criteria from personal interviews of an entire epidemiologic sample, 2.8% of female twins born in the Commonwealth of Virginia received a lifetime diagnosis of bulimia. Our results are within the general range of previous estimates using *DSM-III* and *DSM-III-R* criteria. (While several studies suggest that *DSM-III* criteria for bulimia are broader than *DSM-III-R* criteria [2, 10], others have found little difference in caseness defined by the two criteria sets [5, 40].) It is plausible that true differences exist in lifetime rates for bulimia across populations and/or age groups, but further research will be needed to demonstrate this conclusively. However, our estimate of lifetime risk for *DSM-III-R* bulimia in women of 4.2%, increasing to 8.0% if probable bulimia-like syndromes are included, supports the importance of this syndrome from a public health standpoint.

Methods of Weight Loss

In our epidemiologic sample of bulimic women, 40% of women with narrowly defined bulimia reported self-induced vomiting and 30% laxative abuse. These figures are considerably lower than those reported in clini-

cal samples (41) but similar to those previously reported in nonclinical populations (5, 8). These results suggest that bulimics with deviant methods of weight control (i.e., vomiting or laxative abuse) are more likely to be seen in psychiatric settings than those who use normal weight control methods (i.e., dieting and exercise).

Age at Onset and Cohort Effect

In our population-based sample, the mean age at onset for bulimia was about 20 years, several years later than that reported in samples obtained from clinical settings (37, 41, 42). This discrepancy may result from a greater tendency for subjects with early-onset bulimia to seek treatment.

While it is often stated that bulimia is becoming more common, empirical support for this view is slight. Three studies found evidence for increasing (8), decreasing (43), or stable (44) rates of bulimia during the 1980s. When we divided our sample into three birth cohorts (before 1950, 1950–1959, and after 1960), we found that the later the cohort of birth the higher the risk for bulimia and the earlier the age at onset. These results are similar to those recently reported from a general population sample in New Zealand, where the lifetime prevalence for *DSM-III* bulimia nervosa in women was much higher in younger than in older age groups (5).

This pattern of results is consistent with a cohort or period effect for bulimia. However, because our data, as well as that of the New Zealand sample (5), were gathered retrospectively at one time, the pattern of findings could be explained by two artifacts: a cohort effect for greater awareness of bulimia as a "disorder" and time-dependent forgetting. Older women who experienced bulimia might be less likely to identify it as a "disorder," and hence less likely to recall and report it, than similarly affected younger women. Alternatively, given that onset of bulimia is usually in young adult life, older women will, compared to younger women, have a longer time span in which to forget bulimia. Only prospectively gathered data can powerfully discriminate between real and artifactual explanations of the cohort variations observed for bulimia.

Comorbidity

Most previous studies of comorbidity in bulimia have examined clinical samples. Because individuals with two disorders are more likely to present for treatment than individuals with one disorder, comorbidity may be exaggerated in clinical populations (45). In our nonclinical sample, we documented significant comorbidity between bulimia and a wide range of psychiatric disorders. Contrary to the opinion of some (37–39), our results were not consistent with a special etiologic relationship between bulimia and depression. While a large proportion of patients with bulimia had a history of major depression, this disorder also had a high base rate in the sample. The odds ratio between bulimia and depression was modest and

lower than for most other psychiatric disorders examined. Contrary to most (36, 38) but not all (14) studies done in clinical settings, we found that in most subjects with lifetime diagnoses of both major depression and bulimia, the onset of bulimia followed rather than preceded that of major depression.

Consistent with previous reports (14, 38, 41), we found significant comorbidity between bulimia and both alcoholism and anxiety disorders. The highest odds ratio was found for anorexia nervosa, suggesting some shared etiologic features in these two eating disorders. Our results, however, are consistent with both clinical series (41) and population-based studies (5, 6, 8) in suggesting that only a small minority of patients with bulimia also have a history of anorexia nervosa.

Social Class

Preoccupation with weight and body image is positively associated with social class (46). It has been claimed that boarding schools and colleges may "breed" bulimia (47). However, in our population-based sample, we found no strong evidence for a relationship between bulimia and social class. College attendance was not associated with an increased risk for bulimia. These results are consistent with previous epidemiologic (3) and clinical (48) studies that also found no relationship between social class and bulimia or bulimic behaviors.

Personality

The level of extraversion of bulimic women did not differ from that of the overall sample, while they had, on average, a considerable elevation in neuroticism. These results are broadly consistent with previous clinical (49–51), psychometric (46), and epidemiologic (3) studies that report an association between personality dysfunction and bulimia or bulimic behavior. Given the reported association between avoidant personality disorder and bulimia (50, 51), we were surprised to find no association between levels of introversion and risk for bulimia in our subjects.

Self-Esteem, Body Size, and Image

Bulimia most often occurs in individuals with normal weight, but it is also seen in underweight and overweight individuals (37). Although several researchers have found an association between obesity and bulimia (52, 53), in our general population sample, current weight, body mass index, previous heaviest weight, and usual body silhouette were not related to risk for bulimia. However, bulimic twins had significantly greater previous weight fluctuations and rates of dieting. These results support previous findings that dieting may be a risk factor for bulimia (46, 54).

Level of exercise in our sample was strongly related to risk for bulimia. Eating disorders appear to cluster in certain vocational groups, including athletes (46). Ath-

letic activity in adolescents has been reported to be associated with dissatisfaction with body weight and image (55).

Consistent with results from both clinical (46, 56) and epidemiologic (4, 8) samples, bulimic twins in our sample had significantly slimmer ideal body images than nonbulimic twins. Risk for bulimia was also related to low levels of self-esteem and an external locus of control. These findings support previous research in women linking self-esteem to body image satisfaction (57–59) and bulimia to a high need for approval from others (60, 61).

Parents and Risk for Bulimia

Research based on clinical samples has often hypothesized that parental expectation and a disturbed parent-child relationship are critical etiologic factors in eating disorders (12, 62). Although limited in scope, results from our population-based sample provided little support for these hypotheses. Parental social class was unrelated to the risk for bulimia, suggesting that a greater parental demand for thinness, which is positively associated with social class (63), is unlikely to be of etiologic importance in this syndrome. Risk for bulimia was also unrelated to maternal or paternal body image as reported by the twin; it is therefore unlikely that bulimia is caused by either a reaction formation against parental obesity or a striving to match the body image of a thin parent (3, 46). Contrary to research that has emphasized the role of disturbed mother-child relationships in eating disorders (12, 62), of the four dimensions of parental behavior retrospectively reported by the twins, only paternal care correlated significantly with risk for bulimia.

The Role of Genes in the Etiology of Bulimia

Previous family studies have disagreed as to the presence or magnitude of familial aggregation for bulimia. Two small sample twin studies reported substantially higher concordance rates for bulimia in monozygotic than dizygotic female twins (16, 17). Most previous family or twin studies of bulimia have been uncontrolled, have relied on only indirect or self-report information, or have ascertained their sample through treatment facilities or by advertisement. In the present population-based sample, all twins were personally interviewed by mental health professionals and no interviewer ever evaluated both members of a pair. We tested for bias in the twin method in several ways. The risk for bulimia was unrelated to zygosity, similarity of childhood environment, or frequency of contact as adults. Our results support the validity of the "equal environment assumption" of the twin method with respect to the risk for bulimia.

Consistent with previous reports (17, 18), proband-wise concordance in our sample was substantially higher in monozygotic than in dizygotic twins for both narrowly and broadly defined bulimia. Model fitting

was then applied to both definitions; the best-fitting model in each case suggested that about 50% of the variance in liability was due to additive gene action and 50% to individual-specific environment. However, because of the small number of affected twins, the statistical superiority of this model over a model in which twin resemblance was due to familial-environmental factors was modest. Model fitting results therefore need to be interpreted with caution. Although we do find evidence consistent with genetic influences on risk for bulimia, the evidence against an effect of familial-environmental factors is relatively weak. Given our sample size of affected twins, if genetic factors are significant, we have almost no statistical power to detect an additional modest familial-environmental effect (64).

Bulimia Nervosa and the Bulimia-Like Syndrome

Several epidemiologic investigations have observed a spectrum of bulimic behaviors in which "subsyndromal" cases are at least as common as cases meeting full diagnostic criteria for bulimia (2–5, 8, 11). Consistent with these findings, in our sample, cases of possible bulimia were slightly more common than cases judged to meet full *DSM-III-R* criteria for bulimia nervosa. These possible cases most frequently failed to meet criterion D; while the subjects had the clinical features of the bulimic syndrome, their binges were less frequent than two per week for 3 months.

A focus of this report was therefore to examine, from an epidemiologic and genetic perspective, the relationship between these bulimic-like syndromes and classic bulimia nervosa. Our results were clear-cut. All the epidemiologic risk factors that affected classic bulimia nervosa influenced the risk for the bulimic-like syndrome to a similar degree. The putative period or cohort effect was nearly identical for the two syndromes. A multiple threshold model which hypothesized that the two syndromes reflected different levels of severity on the same continuum of liability fit well in both monozygotic and dizygotic twins. These results consistently support the spectrum concept of bulimia. A bulimic-like syndrome with binge eating episodes less frequent than twice per week for 3 months may differ quantitatively but does *not* appear to differ qualitatively from the classic disorder of bulimia nervosa.

Limitations

The results of this report should be interpreted in the context of four potential limitations. First, twins may not be representative of the general population with respect to eating disorders. Although studies have suggested no differences in the overall rate of psychiatric disorder in twins and singletons (65, 66), no study has specifically compared rates of eating disorders in these two populations.

Second, selection of our sample may not be random with respect to bulimia. Although we began with a register of all twins born in Virginia, those who migrated

out of state or who did not return our initial questionnaires are not represented. However, the refusal rate at the personal interview stage was low and appeared to be unrelated to risk for bulimia.

Third, the associations reported between risk for bulimia and personality traits and weight history are correlational and may not be causal. While several of these measures were obtained years before the personal interview, in many cases this was still after the reported onset of bulimia. Poor self-esteem, neuroticism, or a history of weight fluctuations may predispose an individual to bulimia. Alternatively, bulimia may predispose an individual to poor self-esteem, neuroticism, and weight fluctuations.

Finally, the analyses presented are incomplete. Our goal here was to outline the major features of the epidemiology and genetics of bulimia in our sample. Many of our potential risk factors (e.g., neuroticism and low self-esteem) are probably highly correlated, and a full treatment of these relationships would require multiple regression techniques, as well as the addition of other potential risk factors on which we have information, including symptoms of anxiety and depression, coping behavior, alcohol intake, and parental history of psychiatric illness. Our genetic analyses are also incomplete. In particular, it will be of great interest to employ multivariate genetic analysis to examine the relationship between bulimia and the other major comorbid conditions, including depression, alcoholism, and anxiety disorders. If the sample size is sufficient, these methods will allow us not only to determine whether these disorders share familial risk factors, but also to estimate the degree to which such shared factors are the result of genes or family environment.

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Neurasthenia and Chronic Fatigue Syndrome: The Role of Culture in the Making of a Diagnosis

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Chronic fatigue syndrome is an increasingly popular diagnosis consisting of multiple psychiatric and somatic symptoms. It bears a striking resemblance to the nineteenth-century diagnosis of neurasthenia. Both disorders arose during periods characterized by a preoccupation with commerce and material success and major changes in the role of women. They illustrate the role of culture in the development of a new diagnosis that emphasizes a "medical" rather than "psychiatric" etiology. The authors argue that chronic fatigue syndrome will meet the same fate as neurasthenia—a decline in social value as it is demonstrated that the majority of its sufferers are experiencing primary psychiatric disorders or psychophysiological reactions and that the disorder is often a culturally sanctioned form of illness behavior.

(Am J Psychiatry 1991; 148:1638–1646)

There has been much interest in the recently defined chronic fatigue syndrome. This has been related partly to reports of its growing frequency and substantial morbidity and partly to discussions of its presumed pathogenesis. This interest has been fueled by debates about the role of emotional factors in the syndrome and controversy as to whether the syndrome exists as a discrete entity (1–4). Many clinicians have suggested that chronic fatigue syndrome is no more than George Beard's neurasthenia of the nineteenth century, and this proposition is now coming under careful scrutiny (5, 6). The implication of this argument is that neither chronic fatigue syndrome nor nineteenth-century neurasthenia is a definite syndrome but, rather, they represent explanatory labels for a wide variety of functional somatic symptoms. Wessely (5) has argued that the popularity of both diagnoses results from the emphasis on a nonpsychiatric explanation of symptoms.

In the present paper we extend the recent work of Wessely (5) and Greenberg (6) by more closely examining the sociocultural aspects of chronic fatigue syndrome and neurasthenia and the ways in which both diagnoses reflect the major popular and professional interests of their eras. Particular attention will be paid to the role of attributions and culture, and we will propose explanations for the preponderance of women among patients with these diagnoses. We will focus on the initial North American work related to neurasthenia and will not describe the development of the concept of neurasthenia in Europe (5, 7) or the rapid disappearance of the syndrome over the early years of the twentieth century, which have already been elaborated elsewhere (5–8).

OVERVIEW OF CHRONIC FATIGUE SYNDROME AND NEURASTHENIA

Chronic Fatigue Syndrome

Chronic fatigue syndrome is a constellation of clinical symptoms including incapacitating exhaustion or fatigue associated with a marked reduction in activity level; in addition to the general fatigue, severe fatigue is typically produced by low levels of exertion, which would have been easily tolerated in the premorbid condition but now result in marked fatigue lasting more than 24 hours. Other symptoms include malaise, muscle and joint pain, muscle weakness, feverishness that is usually subjective but may be accompanied by a low-grade temperature elevation, recurrent sore throats, swollen or tender lymph nodes, headaches, and a variety of "neuropsychological" complaints that include dizziness or lightheadedness, nonspecific visual distur-

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Supported by a Career Development Fellowship from the Canadian Psychiatric Research Foundation and by Ontario Ministry of Health Research Personnel Development Program Fellowship 02762 to Dr. Abbey. The results and conclusions are those of the authors, and no official endorsement by the Ontario Ministry of Health is intended or should be inferred.

The authors thank Drs. Donna Stewart and Zbigniew Lipowski for their suggestions, Professor Edward Shorter for guidance regarding the historic literature, Dr. Irving Salit for research collaboration, and Sonia Hollins, Jennifer Bayne, and the staff of the Fudger Health Sciences Library, the Toronto Hospital, for their help.

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bances, irritability, depression, anxiety, and problems with memory, attention, and concentration (1, 9, 10). Holmes et al. (10) have developed case definition criteria for chronic fatigue syndrome to aid researchers in identifying more homogeneous groups of subjects.

Patients with chronic fatigue syndrome report a marked reduction in their functional capacity—most are unable to continue with full-time work, and many receive some form of disability payments for an extended period. They typically report a marked impairment in their interpersonal relationships, and they are unable to pursue formerly pleasurable avocational activities.

There has been little systematic study of the natural history of chronic fatigue syndrome. The onset of the syndrome may be acute or gradual; it has been suggested that a history of acute onset is more likely to be associated with chronic fatigue syndrome, but we know of no data to substantiate this clinical observation. Two patterns of the illness have been described: 1) continuous illness with very slow improvement and 2) recurring relapses and periods of improved function (9). Initially, it was reported that most patients improved within 2 years (9), but there are now many reports of much longer periods of illness. It is unclear whether these patients have more severe forms of chronic fatigue syndrome or whether they are suffering from another disease or illness.

Neurasthenia

Neurasthenia entered the medical literature in 1869, when Beard (11) described a series of 30 cases and argued for the existence of a disorder that explained an array of symptoms which had long perplexed both patients and physicians. He drew the name from Greek and noted that its literal interpretation was “lack of nerve strength” (12, p. vi). In an 1880 monograph, Beard enumerated over 75 symptoms of the syndrome and argued, “Each case of neurasthenia is a study of itself” (12, p. 133). In subsequent monographs (13, 14), he enumerated further symptoms, which included exhaustion, a variety of pains, alterations in the senses, “morbid fears,” impairments in cognitive functioning, and alterations in mood. Beard noted, “These diseases I bring into one family, because they have a common pathology, a common prognosis, a common history, and a common treatment” (12, p. 3).

Interest in similar symptoms (7) had been expressed before Beard’s works appeared, and the word “neurasthenia” had been in medical dictionaries for decades before Beard’s 1869 article (7, 15). In fact, the concept of neurasthenia was independently advanced by Van Deusen in 1869 (16). He reported his observations of farm women admitted to his asylum who had experienced neurasthenia before the onset of their insanity.

Beard noted the difficulties in studying what were primarily subjective states and commented, “Neurasthenia, indeed, has been the Central Africa of medicine—an unexplored territory into which few men enter, and those few have been compelled to bring reports that have been neither credited nor comprehended” (12, p. vi).

Beard further organized the symptoms into subtypes of neurasthenia. Cerebrasthenia (cerebral exhaustion) was characterized by symptoms “that are directly or indirectly connected with the head, and they may be either physical or psychical” (12, p. 106); these symptoms included tenderness of the scalp, a feeling of fullness in the head, disorders of the eyes and ears, and emotional symptoms. Myelasthenia (spinal exhaustion) was defined by symptoms attributed to involvement of the spinal cord, including local muscle spasms, pains in the back and feet, sexual difficulties, and sensitivity to cold and changes in weather. Over time, other authors elaborated further subtypes, the most prominent of which was digestive, or lithemic, asthenia; this was marked by nervous dyspepsia and an overindulgence in food and wine. Physicians argued about the differential importance attached to various symptoms and treatment approaches. By the turn of the century, there was an increased interest in the emotional symptoms associated with neurasthenia and the potential role of emotional factors in its etiology (17).

Many of the symptoms listed by Beard would now be seen either as part of definable psychiatric disorders (e.g., phobias, panic disorder, affective disorders, psychosis) or as organic diseases or psychophysiological symptoms. There remain, however, a number of symptoms with no clear pathogenesis that are similar to the symptoms reported with chronic fatigue syndrome.

Overlap

To demonstrate the considerable overlap between the two diagnoses, descriptions of the two disorders will be contrasted in terms of symptoms in the case definition criteria for chronic fatigue syndrome (10).

Fatigue is the hallmark of the current case definition of chronic fatigue syndrome and was described by Beard with words similar to those of current sufferers: “attacks of a sensation of absolute exhaustion” (12, p. 66) often accompanied by the feeling that the exhaustion is so extreme that one experiences a “going-to-die” feeling (12, p. 66). The result of the exhaustion was that “neurasthenic patients cannot depend upon themselves. One day they can do with impunity what on the following day brings about distressing results” (12, p. 66). Beard’s patients noted, as chronic fatigue syndrome sufferers do today, “When planning to go upon a journey or to undertake any responsibility of any kind, they cannot tell a day beforehand whether they will be equal to it” (12, p. 66).

Mild fever and chills were also described by Beard, who noted the occurrence of “general and local chills and flashes of heat” (12, p. 68) and observed that “attacks of chills in many respects resembling chills and fever . . . are often experienced by a certain class of neurasthenia sufferers” (12, p. 69).

Sore throat was not described in Beard’s first monograph, but he later commented on the prominence of chronic catarrhs, including catarrh of the nose and the nasopharynx. He noted that catarrh was not strictly a

nervous disease but that "in the marked and obstinate forms it is . . . one of the signs or one of the nerve symptoms of . . . [a] decrease in vital force" (13, p. 61).

Muscle aches and pains are a frequent symptom of chronic fatigue syndrome, and Beard noted that "one of the most frequent complaints among the neurasthenic (myelasthenic form) is heaviness and vague aching of the loins and limbs, and sometimes of the whole body" (12, p. 55). He cautioned, "This is a symptom hard to define in exact words, but it is very common, and it is a cause of great distress" (12, p. 55). As with patients today, "This symptom is quite apt to follow over physical exertion, as in walking or standing, but may come on without any apparent or special exciting causes" (12, p. 55).

Generalized headaches different in type, severity, and pattern from headaches in the premorbid state are the seventh minor symptom criterion of chronic fatigue syndrome. Beard described the "sick headache" and argued that it represented "both a symptom and a safety-valve" because he believed the sick headache allowed the nervousness "to manifest itself" and that it "saves other and worse affections" (12, p. 17). Other forms of head pain, pressure, and heaviness were also recognized and were usually, but not always, attributed to vascular congestion of the brain. "Lightness of the head" was also described, and, as with chronic fatigue syndrome sufferers, it was defined by "I cannot tell how I feel" (12, p. 17).

The migratory arthralgias without joint swelling or redness associated with chronic fatigue syndrome were described by Beard, who noted, "Neurasthenia also may simulate rheumatism, and is frequently mistaken for it" (12, p. 105).

Neuropsychological complaints are prominent in chronic fatigue syndrome and "include one or more of the following: photophobia, transient visual scotomata, forgetfulness, excessive irritability, confusion, difficulty thinking, inability to concentrate, depression" (10, p. 389). Many of these symptoms echo the descriptions of neurasthenia. Beard described a number of visual symptoms, including attacks of "dimness of vision" (12, p. 19) and "floating specks before the eyes" (12, p. 20), and he noted the preference for the dark by sufferers, who were troubled by "how irritating to the brain are the ordinary waves of light and sound" (12, p. 139). Impaired concentration was described by Beard as a "notable symptom" (12, p. 22), and he observed that "the mind wanders away in every direction, and when brought back by an effort of the will, is liable to be soon again lost in reverie" (12, p. 23). Difficulty in finding words was reported by a number of his patients and is noted by patients with chronic fatigue syndrome. Beard observed that memory was "often temporarily weakened, and consecutive thought and sustained mental activity frequently impossible" (12, p. 102). He described the irritability as the patient's being in "a condition to fret and worry and become irascible over trifles which, when feeling well and calm, would have no influence upon him" (12, p. 24), and he noted that when "appearing in one previously good-tempered, and associ-

ated with other neurasthenic symptoms it becomes of diagnostic value" (12, p. 24). "Habitual mental depression" (12, p. 102) was described by Beard as "the terrible symptom, mental depression, which drives some of these cases almost to suicide" (12, p. 119). He noted the importance of hopelessness and contrasted the hopelessness of the neurasthenic patient with the retained capacity for hope in patients dying of consumption or cancer (12, p. 24). He attributed the hopelessness to "an instinctive consciousness of inadequacy for the task before us. We are hopeless because our nerve force is so reduced that the mere holding on to life seems to be a burden too heavy for us" (12, p. 25).

Sleep disturbance is a symptom of chronic fatigue syndrome that was also described by Beard: "Nervously exhausted patients often wake up in the morning, feeling almost as tired as when they went to bed in the night. . . . They have not rested by the sleep; they get up tired and discouraged" (12, p. 45). He reported daytime drowsiness and noted that it did not always lead to sleep: "The patient is simply dull, heavy, sleepy, without having the ability to get asleep" (12, p. 46).

The only criterion from the case definition of chronic fatigue syndrome that Beard did not discuss is the experience of painful lymph nodes in the cervical or axillary distribution.

Other commonly described symptoms of chronic fatigue syndrome that are not part of the case definition do overlap with the symptoms of neurasthenia. Many patients with chronic fatigue syndrome comment on their inability to tolerate a variety of substances that they previously enjoyed, such as caffeine, alcohol, and tobacco. Beard commented on the "inability to bear certain kinds of stimulants and narcotics to which the patients have been accustomed" (12, p. 49). Similarly, he commented on the sensitivity to drugs and the need to use markedly lower doses (13, p. 39), a finding common to many patients with chronic fatigue syndrome. A tendency to atopy and various forms of allergies has been noted by Straus et al. (18). Beard described similar findings and frequently emphasized his observation that hay fever is a "sequel" of neurasthenia (12).

RELATIONSHIP OF DIAGNOSIS TO DOMINANT SCIENTIFIC MODELS

The relationship between science and social thought is complex and variable (19). Rosenberg stated that "most aspects of social thought in any culture deal with universal human problems, problems which must be answered by each generation in its own way" and that prominent among these are problems related to sickness and health (19, p. 4). Since the nineteenth century, social thought has been increasingly inspired by science, and metaphors drawn from science have been used to explain a variety of human problems. Mora commented that the ideas regarding causation and the forms of treatment which should be applied to an illness are "closely related to particular beliefs and attitudes

prevailing in a particular society at a particular period" (20, p. 58). This relationship can be seen in the approaches taken in explanations of the symptom complexes of neurasthenia and chronic fatigue syndrome. Rosenberg observed, "Beard was neither a profound nor a critical thinker. His medical writings are a mosaic of the fashionable and controlling ideas of his time, it was the familiarity rather than the novelty of Beard's theories which made them so easily and rapidly accepted" (21, p. 245). Numerous medical historians (8, 19, 21–25) have studied neurasthenia as a model, which Sicherman noted "so neatly illustrates the interplay of scientific theory and cultural values in the fashioning of a disease entity" (22, p. 37).

It can be argued that, just as neurasthenia was a compilation of ideas which captivated the imagination of both the public and medical professionals, chronic fatigue syndrome is also built on two of the most interesting areas in modern medicine—infectious disease and immunology. Most recently, concerns about the contributions of environmental pollution to chronic fatigue syndrome have gained prominence as a result of clinical ecologists' active role in treating patients with the syndrome.

Neurasthenia

Explanations regarding the basis for neurasthenia focused on four major themes of scientific interest during the latter part of the nineteenth century: electricity, conservation of energy, reflex action, and evolution and heredity (6–8, 19–23). Drinka noted that the combination of "nervous exhaustion, electricity and evolution caught the mood of late nineteenth century America and won wide acclaim, both among doctors and the lay public" (7, p. 190).

The electrical nature of the nervous impulse was described by DuBois-Reymond (26) and Helmholtz (7, 19, 21) in the 1840s. Interest in the role of the nervous system in the production of a variety of different symptoms increased after the American Civil War, which provided a vast supply of soldiers with nerve injuries and gave birth to the subspecialty of neurology (22, 25). At the time, the neuron theory did not yet exist and it was thought that the nervous system operated through a fixed quantity of nervous energy, presumably electrical, which continuously flowed through a closed system of channels (7, 19, 21). The interest in the role of electricity in neural transmission was fostered by Beard's work with Edison (27) and was further stimulated by the widespread interest in Edison's invention of the electric light bulb and the widening use of the telegraph and the telephone (7). This interest in the electrical basis of neural transmission was combined with Helmholtz's first law of thermodynamics, the principle of conservation of energy (6, 7, 19, 21), which was described in 1847; it was popularized by the 1870s and was used as the basis for analogies in a wide range of social and historical thinking (19, 21). Beard stated that humans had a finite supply of energy and new energy could not

be generated although it could be transferred through the electrical therapies. When the nervous supply was overspent there was thought to be a "molecular disturbance," probably by the central nervous system's becoming "dephosphorized" (11, p. 218).

One of the major problems in producing a coherent theory of neurasthenia was the diversity of symptoms associated with the disorder. Beard used the theory of "reflex irritation" to organize the disparate collection of symptoms into one disease. Theories of the reflex action or reflex arc model of the nervous system developed in the 1830s (7), and by the 1870s and 1880s "reflex irritation" was described as "a ubiquitous pathological mechanism, helping to explain those ailments in which there was no discernible anatomical change" (21, p. 251). Beard (12) argued that there were three major reflex centers—the brain, digestive system, and sexual organs—and that excessive activity in any one system could deplete the others or an irritative lesion in one system could produce symptoms in the others. This component of the neurasthenia model became the basis for the argument that masturbation or gynecological pathology produced neurasthenia. Beard extended the concept by arguing that mental fatigue or weakness of the nervous system could produce symptoms in other bodily systems on the basis of reflex irritation (21, 22).

The final major theme used in building a theoretical model of neurasthenia was evolution and heredity. Darwin and his theory of evolution, which was published in 1859, had gripped the popular imagination and came to form part of the explanation for neurasthenia (7, 21). Drinka (7) described Spencer's role in applying these concepts to society and arguing that evolution took place in the capitalistic marketplace society, thus making North America highly evolved and most susceptible to the strains of modern civilization. Beard's social Darwinism argued that the higher classes, who were the victims of neurasthenia, were predisposed by the sensitivity of their highly evolved nervous systems (21). The thought of neurasthenia in the "savage" was dismissed as absurd (13). Heredity was invoked to explain the variation in nervous force between individuals, and its role in neurasthenia was discussed by a number of authors (12, 13, 28–30). Collins and Phillips, who noted that 50% of the 333 patients they had studied reported a history of "nervous disease or diathesis" in a family member, summarized the role of heredity as follows: "If one is born with a nervous system that is deficient in the capacity to produce neural energy or, what is the same thing, to maintain a proper equilibrium between production and expenditure of such energy, such a person is far more liable to develop neurasthenia as the apparent result of any of the exciting causes" (29, p. 414).

These four themes come together in Beard's writings: "The force in this nervous system . . . is limited; and when new functions are interposed in the circuit, as modern civilization is constantly requiring us to do, there comes a period, sooner or later, varying in different individuals, and at different times of life, when the

amount of force is insufficient to keep all the lamps actively burning; those that are weakest go out entirely, or, as more frequently happens, burn faint and feebly—they do not expire, but give an insufficient and unstable light” (13, p. 99). The particular components unique to American civilization that were “overloading the circuits” were “steam power, the periodical press, the telegraph, the sciences and the mental activity of women” (13, p. 96). Beard summarized his beliefs about the causes of American nervousness by means of an “algebraic formula as follows: civilization in general + American civilization in particular (young and rapidly growing nation, with civil, religious, and social liberty) + exhausting climate (extremes of heat and cold, and dryness) + the nervous diathesis (itself a result of previously named factors) + overwork or overworry, or excessive indulgence of appetites or passions = an attack of neurasthenia or nervous exhaustion” (13, p. 176).

Over the years, a number of other causes were advanced for neurasthenia. Autointoxication will be briefly described because of the parallels with chronic fatigue syndrome. Rockwell (31) suggested that both physical and mental labor brought about cellular changes at the level of both the brain and the muscle. He argued that there was a “regressive metabolism of tissue of an oxidative character” and that “the poisonous material set free acts upon the muscles through the circulation and weakens them.” The theme was taken up by Deale and Adams (28), and a variety of treatments were advocated, including “rectal alimentation” and various dietary regimens that focused on detoxifying the patient. Kellogg (32) argued for the important role of hydrotherapy in detoxification.

Chronic Fatigue Syndrome

Infectious diseases and their treatment and the new science of immunology have been the most dramatic landmarks in North American medicine since the middle of the twentieth century (33). Thus, it is not surprising that etiological theories of chronic fatigue syndrome have been couched in these terms despite the relative paucity of strong supporting laboratory evidence. Whereas Beard's neurasthenic patients suffered from depleted stores of nervous energy, the twentieth-century patient with chronic fatigue syndrome is reported to be the victim of a weakened immune system and ongoing viral infection.

Initially, chronic Epstein-Barr virus infection was implicated (34–38), but more recent work (39, 40) has demonstrated no correlation between serological markers of Epstein-Barr virus and clinical condition. In the wake of the failure to document a role for the Epstein-Barr virus in chronic fatigue syndrome, workers turned to the newly discovered human herpesvirus-6 (41). However, a recent controlled study (40) showed no difference in prevalence or titers of antibody to human herpesvirus-6 between patients and control subjects. Attention is now focused on the role of the enteroviruses (42, 43), although these studies have also been

inconclusive (44, 45). At present the search for a viral cause continues, and it has been suggested that the virus is a new one not yet isolated.

The second major theme in attempts to explain chronic fatigue syndrome has been immune dysfunction. A variety of disorders of both humoral and cell-mediated immunity have been postulated to cause chronic fatigue syndrome, but such disorders have not been found consistently across studies, occur in only a subset of patients, often overlap with findings in asymptomatic comparison subjects, and have not been demonstrated to correlate with clinical condition (1, 46). Attempts are being made to draw parallels between AIDS and chronic fatigue syndrome in order to legitimize the diagnosis of chronic fatigue syndrome and mobilize political and financial support for research and treatment (47). Some are arguing that it is “a sister illness” of AIDS (48) or “an AIDS epiphenomenon” (Cheney, cited in 48, p. 69). Chronic fatigue syndrome has been described as “the disease of the '90s” (49).

The most recent theme surfacing in the popular and self-help literature on chronic fatigue syndrome is the role of toxins, both external environmental or dietary toxins and internally generated autointoxicants. Toxins have also been implicated in two other poorly defined syndromes characterized by nonspecific somatic symptoms and emotional distress—environmental hypersensitivity syndrome and systemic candidiasis—and reflect our society's growing awareness of the effect of pollution and concern about the possible health effects of environmental contaminants (50, 51). Clinical ecologists have entered the diagnostic arena, bringing with them a variety of beliefs about the impact of the late-twentieth-century lifestyle on health, particularly the effects of widespread antibiotic use, diets with excessive refined sugars and yeasts, and air and soil pollutants (52). All of these factors are invoked as causative agents through a variety of mechanisms, including weakening of the immune system and autointoxication. In a manner reminiscent of Beard's arguments about the uniqueness of the late-nineteenth-century American, it is argued that “the average citizen of the 1980s is biochemically and genetically different from the average citizen of the 1950s. . . . Ordinary medical texts are geared to treat people who no longer exist” (A.S. Levin, cited in 52, p. 4).

Common Theme

Both neurasthenia and chronic fatigue syndrome share the theme of overloading the body's natural reserves—the former in terms of the nervous energy supply and the latter in terms of the immune system. In each case, the overloading is attributed to factors in the contemporary lifestyle. Each developed in an era characterized by public concerns about the fast pace of life and the changing role of women. Beard's descriptions (13) of the stress associated with changing patterns of business and the rapid dissemination of information due to the introduction of the telephone and telegraph could pass for current commentary if computers, fax

machines, and televisions were substituted. Beard wrote about the impact of the new technologies on merchants and the economic system and the ever-increasing need for speed in business transactions. He argued that before the telegraph was introduced merchants transacted business more slowly and were not troubled by rapid price fluctuations, "which now are transmitted instantaneously over the world" and have become the "tyrants of trade" (13, p. 105). The parallels with the present are clear. Both time periods are characterized by an emphasis on financial success and on the application of personal effort and willpower for the acquisition of money, power, and status. Gilbert (53) described this as the "success motif" and discussed its role in neurasthenia. The two periods also share what Drinka has labeled the "Prometheus myth," that is, destruction (i.e., exhaustion) from "reaching too high for the fire of the gods" (7, p. 191). The diagnoses of neurasthenia and chronic fatigue syndrome have provided refuges for those overwhelmed by the battle: "Neurasthenics were provided with a justifiable 'right to be sick' (physical cause) if not a praiseworthy one (overwork)" (54, p. 263).

Much of the discussion in the neurasthenia literature of the causative role of the fast pace of urban life at the turn of the century is similar to present-day concerns about "stress" and "burnout." However, each generation has understood the impact in terms of its own theoretical models. To the nineteenth-century physician these life stressors acted through depletion of a limited supply of nervous energy, whereas to the twentieth-century proponent of chronic fatigue syndrome they are the cause of immune dysfunction and heightened susceptibility to prolonged viral infection.

ROLE OF GENDER

Historians have studied the important role of gender in the social construction of the diagnosis of neurasthenia. Women were overrepresented among the sufferers of the disorder, and the reasons for this were the focus of considerable speculation both at the time and today. Men played an important role in making the diagnosis respectable and giving credence to it. The relationship of gender to neurasthenia is interesting and has parallels with chronic fatigue syndrome.

Female sickliness was a prominent feature of the latter half of the nineteenth century. Catherine Beecher, in "Letters to the People on Health and Happiness," commented on the lack of health in women and noted, "I am not able to recall, in my immense circle of friends and acquaintances all over the Union, so many as ten married ladies born in this country and century, who are perfectly sound, healthy and vigorous" (cited in 55, p. 55). Although Beecher considered some of this illness to be sequelae of multiple pregnancies and physical diseases, she noted that the primary problem was lack of vigor and numerous nonspecific somatic symptoms. Her observations were supported by a number of her contemporaries. Feminist historians (56–60) see neurasthenia and the general sickliness of women as a manifestation of women's distress and their lack of satisfaction with life. The rise of neurasthenia occurred in the context of significant changes in the role of women in the new industrial society, the increasing education of women, and the beginning of women's acceptance into the professions (59). This resulted in what Ehrenreich and English (59) have termed "the woman question," i.e., the problem of defining the role of women in a society transformed by the Industrial Revolution. Before industrialization, women had occupied clearly defined and highly valued roles in the home and healing, but with the advent of the factory and the capitalistic marketplace, these traditional roles were no longer valued (59). Showalter (60) also noted the importance of the changing role of women in the development of neurasthenia. She observed that physicians in the late nineteenth century made explicit links between women's ambition and the upsurge in three diseases that occurred predominantly among females—neurasthenia, hysteria, and anorexia nervosa.

Although more opportunities had opened for women, there was still considerable social conflict about the role of women. Many women of the time felt this conflict played an important part in the development of neurasthenia. Dr. Margaret Cleaves, a neurasthenic who wrote the anonymous *The Autobiography of a Neurasthene, As Told by One of Them and Recorded by Margaret A. Cleaves* (30), published in 1910, also wrote a number of essays about neurasthenia in women. She attributed the illness not merely to overwork but more specifically to the thwarted ambitions of women in a society that was unable to fulfill the aspirations of the "new woman." Support for this argument was provided by the writings of a number of highly successful women who suffered from neurasthenia and reported their experiences, including Jane Addams, Charlotte Perkins Gilman, Florence Nightingale, and Edith Wharton (22, 23, 59, 60). Gilman, who had been unsuccessfully treated by Silas Weir Mitchell, identified her own sickliness as a result of her dissatisfaction with her role as wife and mother, noting that she was very symptomatic in the presence of her husband and child but her symptoms vanished when she was away from them (59). These observations were dismissed by Mitchell as "a self conceit," and he suggested that she "live as domestic a life as possible" and prohibited her pursuit of writing (cited in 59, p. 102). Her conflictual relationship with Mitchell served as inspiration for a short story, "The Yellow Wallpaper" (61), which chronicles a woman's descent from nervous exhaustion into a psychotic depression as a result of treatment based on Mitchell's rest cure. The story opens with the woman's observations of her physician husband, who is modeled on Mitchell: "John is a physician, and perhaps—(I would not say it to a living soul, of course, but this is dead paper and a great relief to my mind)—perhaps that is the one reason I do not get well faster. You see he does not believe I am sick! And what can one do? If a physician of high standing, and one's

own husband, assures friends and relatives that there is really nothing the matter with one but temporary nervous depression—a slight hysterical tendency—what is one to do?” (61, pp. 9–10). Ultimately, Gilman left the marital home and pursued her career as a writer, lecturer, and activist, although she continued to be troubled by periods of severe fatigue and lethargy (56). Jane Addams, the pioneer social worker and founder of Hull House, also consulted Mitchell and was also at odds with him as to the explanation of her symptoms, which she attributed to her difficulty in reconciling her ambitions and ideals and using her college education within the social constraints of the time (21). Similar difficulties with physicians were reported by Alice James, who had been treated by a variety of nerve specialists: “I suppose one has a greater sense of intellectual degradation after an interview with a doctor than from any human experience” (cited in 60, p. 144).

Considerable interest focused on the relationship between the reproductive organs and the nervous system and was guided by the dominant theoretical model of the day, “reflex irritation,” which was described earlier. Beard’s extension of the doctrine of reflex irritation to the effect of nervous system activity on the reproductive organs was widely applied and ultimately became part of the debate about the education of women (23, 57–60, 62). He observed, “It seems to be almost impossible for any woman to suffer from general neurasthenia without developing, sooner or later, primarily or secondarily, some trouble of the womb or ovary” (14, pp. 202–203) and advocated the use of “local treatments” to prevent further damage. Numerous physicians argued that studying caused poor functioning of the reproductive organs and might compromise fertility (23, 59, 60). Coleman advised women, “Beware! Science pronounces that the woman who studies is lost” (cited in 59, p. 128). It is interesting that the concept of “reflex irritation” is returning under the twentieth-century guise of interest in the relationship of endometriosis and premenstrual syndrome to chronic fatigue syndrome (63).

Male sufferers of neurasthenia provided the illness with credibility and respectability. Showalter (60) noted that the existence of many male patients made this disorder different from hysteria and anorexia nervosa, which occurred predominantly in females and were seen as not respectable. Neurasthenia was “seen as an acceptable and even an impressive illness for men, ideally suited to a capitalistic society and to the identification of masculinity with money and property” (60, p. 135). The disease was one of overwork and excessive devotion to duty, both desirable qualities in the marketplace, so in some respects the diagnosis was a badge of honor. Many of the physicians initially involved in the study of neurasthenia, including Beard and Mitchell, had personal experience with neurasthenia and were eager to confer respectability on the diagnosis (8, 21–23, 59, 60, 64). Beard (12) noted that at least 10% of his patients were male physicians whose superior powers of observation helped to further knowledge about the disorder. His case histories referred to socially

prominent male business leaders, lawyers, and members of the clergy. Thus, neurasthenia became an ideal illness in that it was both a mark of success (“a certain status and social accomplishment—a feeling of intellectuality and high culture” [23, p. 28]) and a justification for lack of achievement (23, 54, 59, 60). This was important to patients as it allowed them to escape the pejorative diagnoses of hypochondriasis and hysteria.

At present, the diagnosis of chronic fatigue syndrome is more common among women, and there are many parallels with the gender dynamics described for neurasthenia. Our own culture is wrestling with the expanding role of women and the mismatch between women’s ambitions and social possibilities. Clinical experience suggests that among chronic fatigue syndrome sufferers are a number of women and men who feel conflicted about their working lives and the difficulty in balancing their careers with their family obligations and personal wishes. The diagnosis of chronic fatigue syndrome provides a legitimate “medical” reason for their fatigue, emotional distress, and associated psychophysiological symptoms and allows them to withdraw from situations they find intolerable on the basis of illness rather than their own volition. This dynamic has been observed for patients in a number of differing situations, including high achievers who are motivated by pleasing others and in midlife reevaluate their priorities and women who are ambivalent about leaving paid employment to stay home with young children. Illness and the sick role are the only socially legitimate excuse for abandoning the workplace and the pursuit of achievement.

CONCLUSIONS

The parallels between neurasthenia and chronic fatigue syndrome are striking—the two disorders have similar symptoms and arose during decades characterized by preoccupation with commerce and material success and by major changes in the role of women. Both have been labeled medical diseases and explained in terms of the major scientific themes of their day. The history of neurasthenia is fascinating and helps to illuminate some of the complexities surrounding the current diagnosis of chronic fatigue syndrome. Ultimately, out of the heterogeneous matrix of neurasthenia it was possible to identify a number of discrete psychiatric and medical disorders. What remained was a mixture of nonspecific, functional somatic symptoms and psychological distress, which became increasingly unfashionable and disappeared from the clinical scene during the early twentieth century. We argue that the same will occur with chronic fatigue syndrome (65). Although it is possible that a newly described disease will account for the illness in some patients, it seems clear that the majority of patients with a self- or physician-conferred diagnosis of chronic fatigue syndrome are suffering from one or more of the following: an identifiable psychiatric disorder, psychophysiological symptoms sec-

ondary to acute or chronic psychosocial stress, or a form of illness behavior (65). The studies of psychiatric syndromes in patients with chronic fatigue syndrome (4, 40, 66–68) have indicated a high prevalence of psychiatric disorder, most prominently major depression, dysthymia, and somatization disorder. The most common diagnosis is major depression, but the relationship between depression and chronic fatigue syndrome is unclear, i.e., is it cause, effect, or covariate? (69). The potential relationship between these psychiatric syndromes and chronic fatigue syndrome as a form of illness behavior is intriguing (65, 70). Kleinman has studied the relationship between depression, somatization, and social distress in contemporary Chinese neurasthenic patients. In a series of elegant studies (71) and subsequent reflections on this work (70), he persuasively demonstrated the interrelationship of these processes in the construction of neurasthenia, which he considered a “cultural idiom of distress” or a form of culturally sanctioned illness behavior. He noted, “Whether or not the official medical lexicon in a society treats neurasthenia as an authentic *disease*, the syndrome of chronic exhaustion is a ubiquitous *illness* behavior that can be described and interpreted for particular individuals engaged in particular situations and relationships within particular cultural contexts” (70, p. 104). The recognition of the illness behavior component is essential in understanding why, despite pharmacological treatment of the associated psychiatric disorder, neurasthenic symptoms persist (71). Kleinman noted, “Only those patients improved who resolved a major family or work problem” (70, p. 103). This has been our clinical experience in treating patients with chronic fatigue syndrome.

The concept of chronic fatigue syndrome as a form of illness behavior in many patients is supported by the overlap with a wide variety of other diagnoses characterized by multiple nonspecific symptoms. The medical histories of a substantial subgroup of patients with chronic fatigue syndrome are replete with such diagnoses as irritable bowel syndrome, fibromyalgia, premenstrual syndrome, temporomandibular joint syndrome, and hypoglycemia—all of which have spawned controversy about the relationship between “organic pathology,” emotional distress, and illness behavior and all of which are frequently misdiagnosed among the emotionally disturbed (51)—as well as more esoteric diagnoses, such as environmental hypersensitivity syndrome and systemic candidiasis. Stewart (72) described the process by which somatizing patients move between these different diagnostic labels.

As with neurasthenia, the diagnosis of chronic fatigue syndrome, because of its implied “organicity,” is attractive to patients and is tenaciously upheld. Sicherman (22) reviewed nineteenth-century case notes discussing neurasthenic patients’ interpretations of their symptoms and noted the emphasis on external causes. She cited neurasthenic patients who had recently experienced a death in the family and attributed their symptoms of fatigue, ill health, and emotional distress to excessive exposure to cold and rain at the funeral rather than to the psychologi-

cal effects of the loss of a loved one. Psychologically minded clinicians assessing patients self-diagnosed as having chronic fatigue syndrome have seen this scenario repeatedly. The appeal of a “medical” diagnosis serves to remind us of the continued stigmatization of psychiatric illness and emotional distress (5, 73).

Thus, both chronic fatigue syndrome and neurasthenia offer important lessons for psychiatry and medicine, but, rather than offering new vistas on pathophysiological processes, they primarily “illustrate the utility of scientific metaphor and authority in helping rationalize a rapidly changing and stress-filled world” (19, p. 98) and demonstrate the cultural shaping of illness and disease.

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A Psychobiological Perspective on the Personality Disorders

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A preliminary but growing body of evidence supports the existence of genetic and biological substrates of personality, suggesting the utility of a psychobiological perspective on the personality disorders. The investigation of biological correlates of personality disorders can provide an empirical base to explore the relationship between biological predispositions and psychological function. The authors propose a psychobiological model based on dimensions of cognitive/perceptual organization, impulsivity/aggression, affective instability, and anxiety/inhibition. These dimensions span the DSM-III-R axis I and axis II disorders. The authors review phenomenological, genetic, and biological evidence in relation to each of these dimensions. Although such an approach remains heuristic, this model provides a promising vantage point from which to generate investigation of the development and treatment of the personality disorders.

(Am J Psychiatry 1991; 148:1647-1658)

Each ego is endowed from the first with individual dispositions and trends, though it is true that we can not specify their nature or what determines them.

—Freud (1)

Freud's observation more than 50 years ago reflected his increasing appreciation that innate or "constitutional" differences may bias the character and plasticity of an individual's adaptational capacities. Such variations may provide the substrates for the enduring and characteristic patterns of thinking, feeling, and behaving termed "personality" or, if these patterns are sufficiently maladaptive, "personality disorders."

The identification of the specific biological mechanisms underlying these predispositions is now increasingly feasible and represents an important step toward developing a more valid nosology and more effective treatments for the personality disorders. In this article, we present a specific heuristic model of psychobiologically based dimensions of personality disorder and evidence pertaining to this model. This model offers a starting point for biological investigation of the personality disorders and is not intended to accommodate all

the complexities of our knowledge of personality disorders from either a biological or a psychological perspective. It offers an opportunity to integrate clinical observations from such seemingly divergent perspectives as psychoanalysis and behaviorism. We will propose a number of implications of this model for the development and clinical treatment of personality disorders. Although some of the proposed implications are speculative, new investigative strategies generated by this model are suggested to test specific hypotheses.

HISTORICAL BACKGROUND

Biological approaches to personality are not new; they date back to the time of Hippocrates (2, 3). Psychoanalysts have long perceived individual differences in the strength of the "drives" and the choice of defense mechanisms. Psychologists such as Eysenck have documented psychometric dimensional factors in normal personality; these factors have been hypothesized to reflect a genetic/biological basis (4-7).

Recent developments in the clinical neurosciences as well as in the diagnosis of the personality disorders now enable the direct study of biological factors in the personality disorders. Advances in basic neurobiology have stimulated the development of powerful tools to understand the pathophysiology of the axis I disorders, which are now being applied to the DSM-III-R axis II disorders with promising results. Operationalized diagnostic interviews based on specific diagnostic criteria permit the reliable assessment of the personality disorders and have made them a more accessible target of investigation.

Interest in the biology of the personality disorders has

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The authors acknowledge the collaborative research efforts of Emil Coccaro, M.D., Robert Trestman, M.D., Jeremy Silverman, Ph.D., Howard Klar, M.D., Andrew Aronson, M.D., Oren Kalus, M.D., Timothy Lawrence, M.D., and many others, which stimulated the writing of this paper. They also thank John Gunderson, M.D., Philip Holzman, Ph.D., S. Charles Schulz, M.D., Marjorie Klein, Ph.D., and Beatrice Hamburg, M.D., for their helpful comments.

also been bolstered by recent developments in our understanding of child development and genetics. Not only does there appear to be a substantial degree of continuity of temperament from infancy through childhood (8, 9), but studies of twins, including twins reared apart, demonstrate a major genetic influence on personality development, greater than has previously been appreciated (10, 11). Although these studies are based on samples unselected for pathology, personality disorder traits also show familial aggregation (12–17) and, in some cases, have been shown to be significantly heritable (18, 19). The demonstration of robust genetic contributions to personality suggests that biological factors mediating these genetic susceptibilities in the context of ongoing environmental influences may be identified.

CORE PSYCHOBIOLOGICAL PREDISPOSITION

The psychobiology of personality disorder can be formulated as a dimensional model grounded in the major axis I syndromes. This model affords an opportunity to build on several decades of intensive research into the biology and genetics of the major psychiatric disorders and incorporates the advantages of a dimensional rather than categorical approach to the personality disorders (20). The major classes of the *DSM-III-R* axis I disorders include the schizophrenic disorders, affective disorders, impulse control disorders, and anxiety disorders. The core features of the schizophrenic, affective, impulse, and anxiety disorders can be conceptualized as reflecting disturbances in fundamental psychobiological dimensions of cognitive/perceptual organization, affective regulation, impulse control, and anxiety modulation. Abnormalities in these dimensions can occur on a continuum on which extreme, discrete symptoms manifest as an axis I disorder. At the other end of the continuum, milder persistent disturbances on one or more of these dimensions might contribute to the development of specific defense mechanisms and adaptational strategies. If these susceptibilities crystallize to define the pervasive, characteristic ways in which an individual behaves across occupational and interpersonal situations, then that individual can be considered to have an axis II disorder.

For example, the schizophrenic disorders are characterized by disturbances in cognitive/perceptual organization, which are manifest in thought disorder, psychotic symptoms, and social isolation. More subtle disturbances in cognitive controls may be expressed not only as persistent symptoms reflecting cognitive/perceptual distortions but also as traits of eccentricity, peculiar speech, and social detachment, as observed in schizotypal personality disorder, the prototype of the “odd cluster” diagnoses.

The affective disorders are characterized by alterations in the regulation and intensity of mood. The major affective disorders are characterized by relatively sustained, autonomous episodes of mood disturbance. In contrast, more transient, environmentally responsive

affective shifts may interfere with the development of stable relationships and self-image, as in borderline personality disorder.

The impulse control disorders are characterized by a diminished capacity to delay or inhibit action, particularly aggressive action. Poor impulse control may result in episodic impulsive/aggressive behaviors associated with axis I disorders such as intermittent explosive disorder, pathological gambling, or kleptomania. When chronic and pervasive, a predisposition to impulsive/aggressive behaviors may result in persistent self-destructive and antisocial behaviors, as in borderline and antisocial personality disorders.

A dimension of anxiety/inhibition can be defined as a low threshold for subjective fear and autonomic arousal in anticipation of aversive consequences, often associated with behavioral inhibition. Although discrete episodes of anxiety, compulsive rituals, or phobias can be observed in the axis I anxiety disorders, attempts to cope with a pervasively low threshold for anxiety might contribute to the avoidant, compulsive, and dependent behaviors of the “anxious cluster” diagnoses.

Thus, dimensions of personality disorder such as cognitive/perceptual organization, affective instability, impulsivity/aggression, and anxiety/inhibition may be represented as occurring on continua with the phenomenologically corresponding axis I and axis II disorders, and characteristic symptoms, traits, and defenses may be associated with each dimension (table 1). Variations in severity along each dimension and interactions between dimensions can provide a rich biological vocabulary contributing to the many temperamental styles characteristic of the personality disorders. For example, criteria for the “dramatic cluster” disorders include those which reflect both impulsivity/aggression and affective instability. Impulsivity/aggression without prominent affective instability is more characteristic of antisocial personality disorder, and affective instability without impulsivity/aggression can be observed in cyclothymia and some “anxious cluster” diagnoses. Severe personality disorders such as borderline personality disorder are likely to demonstrate disturbances along several of these dimensions.

Although this framework is a heuristic one to facilitate psychobiological investigation, it is congruent with other classification schemata based on psychometric and genetic considerations in defining three to four primary dimensions of personality along similar lines (4–7, 21). For example, anxiety/inhibition, which is also a dimension in Gray's schema (7), might be expected to correlate with high harm avoidance in Cloninger's tridimensional system (21), and impulsivity/aggression, also identified in Gray's schema, might be mapped into low harm avoidance and high novelty seeking. Affective instability may be related to high reward dependence in Cloninger's schema.

These other systems, however, represent attempts to define a comprehensive schema of normal personality derived from psychometric studies of nonclinical populations rather than a schema of abnormal personality

TABLE 1. Phenomenologically Corresponding Axis I and Axis II Disorders, Potential Biological Indexes, and Characteristic Traits (Core Vulnerabilities), Defenses, and Coping Strategies of Dimensions of Personality Disorders

Dimension	Axis I Disorder	Axis II Disorder	Biological Indexes	Characteristic Traits	Defenses and Coping Strategies
Cognitive/perceptual organization	Schizophrenia	Odd cluster (schizotypal personality disorder)	Eye movement dysfunction, ^a continuous performance task, backward masking test, ^a plasma HVA, ^a CSF HVA, ^a evoked potential response, VBR	Disorganization, psychotic-like symptoms	Social isolation, detachment, guardedness
Impulsivity/aggression	Impulse disorders	Dramatic cluster (borderline and antisocial personality disorders)	CSF 5-HIAA, ^a responses to serotonergic challenge, galvanic skin response, ^a continuous performance task	Readiness to action, irritability/aggression	Externalization, dissociation, enactment, repression
Affective instability	Major affective disorders	Dramatic cluster (borderline and possibly histrionic personality disorders)	REM latency, responses to cholinergic challenges, ^a responses to catecholaminergic challenges ^a	Environmentally responsive, transient affective shifts	Exaggerated affectivity, "manipulativeness," "splitting"
Anxiety/inhibition	Anxiety disorders	Anxious cluster (avoidant personality disorder)	Heart rate variability, ^a orienting responses, responses to lactate and yohimbine	Autonomic arousal, fearfulness, inhibition	Avoidant, compulsive, and dependent behaviors

^a Preliminary data are available in patients with personality disorder.

derived from studies of patients with severe personality disorders or axis I disorders. Accordingly, these approaches emphasize schizophrenia-related or affective-disorder-related symptoms less than variations in normal personality. In contrast, the model presented here is designed as a heuristic framework for psychobiological research of the personality disorders using clinical constructs with face validity. The extent of convergence of dimensions of normal and pathological personality disorders remains to be determined. External validity studies in both normal subjects and patients with personality disorders will be required to determine the exact character of dimensions of personality. The model proposed here represents only a starting point for future studies.

The framework proposed here builds on the base of knowledge of the biology of the axis I disorders. Biological measures that have proved useful in investigating the axis I disorders may be evaluated for the corresponding axis II disorders by using both dimensional and categorical assessments of personality disorder. In most cases, the hypotheses generated by such a paradigm remain untested and further research is required to evaluate the commonalities and differences between the axis I and axis II disorders along each dimension. We will review here the available evidence implicating an association of specific biological factors with each of these dimensions and will also discuss the clinical implications of these findings and suggest hypotheses for further research.

COGNITIVE/PERCEPTUAL ORGANIZATION

Definition

The dimension of cognitive/perceptual organization reflects an individual's capacity to perceive and attend

to important incoming stimuli, process this information in relation to previous experience, and select appropriate response strategies. Disturbances in this dimension will be apparent in defects in the attention/selection processes that organize an individual's cognitive/perceptual evaluation of and relatedness to his or her environment. The result may be impairment and discomfort in social interactions and a misunderstanding or suspiciousness of others' motivations. Social isolation may represent the major strategy to cope with defective information processing of social cues. In more severe cases, such individuals may be prone to cognitive/perceptual distortions, amplified by social detachment, which forestalls the possibility of potentially corrective input for reality testing.

Biological Correlates

The inclusion of schizotypal personality disorder in *DSM-III* was based in part on the demonstrated genetic association between schizophrenia and schizophrenia-related personality traits (22). This relationship has stimulated the biological investigation of schizotypal personality disorder using measures that have been used extensively in investigations of patients with chronic schizophrenia.

Tests of attention/information processing have demonstrated abnormalities similar to those of patients with schizophrenia in subjects with schizotypal disorders (23). Eye movement dysfunction has been demonstrated not only in patients with chronic schizophrenia and their relatives (24) but also in schizotypal patients and volunteers (25–27) and has been particularly associated with deficit symptoms in schizotypal patients (23, 26–28). Performance on other tests of visual or auditory attention, such as the backward masking test (23, 29), the continuous performance task (23, 30, 31), and sensory gating tests (23, 32, 33), have also been

reported to be impaired in schizotypal subjects (patients, volunteers, and/or relatives of schizophrenic probands) as well as in schizophrenic patients. These measures also have been associated with deficit symptoms and social withdrawal in schizophrenic patients. Although information processing deficits on some of these tasks have been reported in some studies of patients with affective disorders as well, these abnormalities are more likely to be state-dependent and may be different in character in subjects with affective disorders than they are in schizophrenic subjects (23, 24, 29, 32, 34, 35). These results suggest that schizotypal individuals share an impairment in attention/information processing with patients with chronic schizophrenia which may be associated particularly with the enduring deficit symptoms of the schizophrenia spectrum. Further investigation of this possibility and the specificity of such a relationship is required.

In contrast, indexes of dopamine metabolism, such as plasma homovanillic acid (HVA) (36, 37), are associated with psychotic symptoms in schizophrenic patients. Similarly, higher levels of plasma (38) and CSF (34, 39) HVA in preliminary studies of patients with schizotypal personality disorder than in control subjects are correlated specifically with the psychotic-like symptoms of schizotypal personality disorder. Thus, dopaminergic activity could modulate the expression of an underlying genotype for the schizophrenia-related disorders toward or away from severe psychotic symptoms.

Given the greater prevalence of schizophrenia-related personality disorders than of chronic schizophrenia itself in the relatives of schizophrenic patients, chronic schizophrenia may represent only the tip of the iceberg of the schizophrenia-related disorders. The cognitive disorganization underlying these disorders might be more likely to manifest itself as schizotypal or even milder, related personality disorder traits. Determination of the exact boundaries of the schizophrenia-related spectrum and whether they extend to include individuals with schizoid and paranoid traits in clinical settings or families of patients with schizophrenia requires further investigation.

Treatment Implications

The implications of a psychobiological model for patients with schizotypal personality disorder are two-fold. First, neuroleptics would be expected to benefit the schizotypal patient with psychotic-like symptoms, particularly in periods of decompensation. Indeed, schizotypal psychotic-like symptoms improve with neuroleptic treatment (40, 41). Second, the need of schizotypal subjects for "distance," as a means of managing their limited capacity for interpersonal relatedness and vulnerability to stress, needs to be respected. Such an approach does not preclude acknowledgment and encouragement of the schizotypal individual's desires for more comfortable social interactions through interpersonal learning in individual psychotherapy or social skills training (42).

IMPULSIVITY/AGGRESSION

Definition

Impulsivity/aggression can be formulated as a low threshold for active responses to internal or external stimuli, i.e., motor disinhibition, manifest as a tendency toward action-oriented and aggressive behavioral strategies. Impulsive/aggressive individuals have difficulty anticipating the effects of their behavior, learning from undesirable consequences of their previous behaviors, and inhibiting or delaying action appropriately. They tend to externalize the source of their difficulties, are prone to the excessive expression of aggression and frustration, and may be less likely to experience guilt or anxiety.

A number of the personality disorders of the "dramatic cluster" and borderline personality disorder in particular manifest at least some characteristics related to impulsivity/aggression, although each emphasizes different features of this dimension. For example, in antisocial personality disorder, impulsivity/aggression is manifest in a lack of suppression of aggressive behaviors that defy normal social constraints, such as stealing or lying. In borderline personality disorders, impulsivity/aggression may be expressed as suicide attempts, angry outbursts, fights, and substance abuse, often in response to a disappointment or frustration in an important relationship. Impulsivity/aggression may also contribute to the exaggerated displays of emotion and lack of tolerance to frustration of the histrionic patient and to the disinhibited rage in response to criticism of the narcissistic patient. Impulsive patients tend to use defenses of repression, dissociation, or enactment to avoid the experience of anxiety.

Impulsivity/aggression does not define a single personality disorder but, rather, a dimension of behavior and related defenses that can occur in a range of personality disorders. Indeed, genetic and family history studies suggest a genetic component to antisocial personality disorder, borderline personality disorder, and other "dramatic cluster" diagnoses (13, 15-18). Moreover, these disorders cluster together in families, and the familial aggregation may be better accommodated by a dimension of impulsivity/aggression than by discrete heritable categories (15). Further research will be required to determine whether this dimension is best restricted to disinhibited aggression or to a more encompassing motor disinhibition and its relationship to disinhibition in the cognitive domain (e.g., obsessive-compulsive disorder).

Biological Correlates

A predisposition to impulsive behaviors implies dysfunction of brain systems modulating and inhibiting action and aggressive behaviors in response to environmental stimuli. Studies before the advent of *DSM-III* posited that greater EEG slow-wave activity and a low threshold for sedation discriminate sociopathic indi-

viduals from dysthymic individuals, suggesting lower cortical inhibitory function and reduced arousal in the sociopath (5, 43). Impulsive or sociopathic individuals also show less inhibition of motor responses, weaker sympathetic responsiveness, and more rapid habituation in their skin conductance response than other patient groups (5, 44). These psychophysiological and psychomotor differences between impulsive and non-impulsive personality disorders are consistent with the proposition that impulsive or sociopathic individuals are more likely to respond to important environmental stimuli by motor responses than by an evaluative delay characterized by cortical activation, sympathetic arousal, and an inhibition of motor output.

Preclinical studies suggest that the serotonergic system mediates behavioral inhibition. Lesions of the serotonergic system result in a diminished capacity to suppress punished behaviors. The deficit seems to reside in a loss of the capacity to translate the anticipation of punishment into appropriate behavioral inhibition (7, 45). A concomitant of behavioral disinhibition is a pronounced increase in unmodulated aggressive behaviors, e.g., the unrestrained killing of mice in serotonergically lesioned rats (46).

A similar diminution of serotonergic function appears to be associated with a disinhibition of impulsive and aggressive behaviors in patients with personality disorders. Indeed, reduced concentrations of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) have been reported in both depressed patients and patients with personality disorders who have attempted suicide (47, 48), in patients with personality disorders displaying violent and aggressive behavior (48), and in violent offenders (49). The prolactin response to the serotonergic releasing agent fenfluramine is lower in patients with borderline personality disorder, suggesting diminished serotonergic function (50). Diminished serotonergically mediated responses in patients with personality disorders are specifically associated with impulsive/aggressive behaviors, both self-directed (suicide attempts) and other-directed (fights), but not depression, anxiety, or other behavioral traits. In depressed patients, in contrast, diminished prolactin responses to fenfluramine have been reported (50, 51) but, similar to findings in studies of CSF 5-HIAA in depression, have been more specifically associated with suicide attempts than externally directed aggression (50). Pharmacological agents that enhance serotonergic function may attenuate aggressive acts and suicidal behavior in criminal offenders and psychiatric patients (52, 53).

The noradrenergic system may also be involved in the control of impulsive/aggressive behaviors. Higher levels of noradrenergic metabolites have been found in gamblers and are associated with extroversion in gamblers (54) and with sensation-seeking in volunteer subjects (55). Greater growth hormone responses to the noradrenergic agonist clonidine have also been positively correlated with measures of irritable aggression in a preliminary study of patients with personality disorders (56). Since the noradrenergic system mediates arousal

and orientation to the environment, enhanced noradrenergic activity might be expected to increase the likelihood of externally directed aggression. Impaired noradrenergic transmission, on the other hand, would block other-directed aggression. In fact, in animal studies, concomitant lesions of the noradrenergic system prevent the aggression usually associated with serotonergic lesions (57). In clinical studies, reduced noradrenergic function, as for example in major depressive disorders (58), may contribute to the lack of an association between blunted serotonergic activity and externally directed aggression in depressed patients, while the association with self-directed aggression remains intact (50). The interaction of serotonergic abnormalities with abnormalities in other biological systems may contribute to the differential behavioral correlations with serotonergic abnormalities across the affective, anxiety, schizophrenic, and personality disorders. In the personality disorders, both the noradrenergic and serotonergic systems may be important determinants of impulsive and aggressive behaviors directed toward the self and others.

Treatment Implications

The concept of an underlying biological contribution to impulsive behaviors raises the possibility that pharmacological interventions might have an impact on the treatment of these disorders. Lithium, which enhances postsynaptic serotonergic receptor function, has indeed been reported to reduce aggressive behaviors in criminal offenders (53). Preliminary trials have found that the serotonin reuptake blocker fluoxetine reduces impulsive behaviors and borderline traits (59). Enhancement of noradrenergic activity (e.g., by stimulants or antidepressant treatment) may have a negative impact on impulsivity/aggression, while antiadrenergic agents such as propranolol have been reported to reduce aggressive behaviors (60).

Pharmacological intervention, by reducing impulsive behaviors, may also facilitate psychological change in psychosocial treatment modalities. If such intervention decreased the tendency of patients with "dramatic cluster" personality disorders to enact their conflicts, they might facilitate insight-oriented psychotherapy. An appreciation by the therapist of the action-oriented proclivities of these patients might enhance an empathic but limit-setting approach to them.

AFFECTIVE INSTABILITY

Definition

Affective instability can be defined as a predisposition to marked, rapidly reversible shifts in affective state that are extremely sensitive to meaningful environmental events which might induce more modest emotional responses in other people, such as separation, frustration of expectations, or criticism. Because the de-

veloping representations of self and others may be influenced by affective state, an instability in mood may impair an individual's capacity to maintain a stable self-esteem. Such individuals may develop coping and defense mechanisms to minimize the impact of their affective sensitivity. The character of these defenses may depend on variations in other dimensions. Inhibited, anxious individuals will tend to avoid potentially painful involvements with others. Disinhibited, impulsive individuals may exaggerate their affective responses, using their emotionality to control the behavior of others in order to modulate their own mood and self-esteem. Such individuals often do not perceive their behavior as manipulative but as essential to the maintenance of their affective well-being.

Biological Correlates

Affective instability is a central criterion for borderline personality disorder. Many patients with borderline personality disorder develop depressive episodes (15–17). Probands with borderline personality disorder and a comorbid major depressive disorder have been reported to have a higher prevalence of affective disorders in their relatives (15, 16). In contrast, affectively unstable personality disorders are more prevalent in the relatives of patients with borderline personality disorder whether or not they carry a comorbid depressive diagnosis (15). These results raise the possibility of a heritable, biologically based trait of affective instability that may be partially related to the major affective disorders. The precise relationship of this trait to the classical affective disorders requires further investigation.

Biological data also point to the possibility of a relationship between major depressive disorder and the affective instability of borderline personality disorder (61). Although shorter REM latency is characteristic of major depressive disorder, patients with borderline personality disorder also have been reported to demonstrate shorter and more variable REM latencies (61, 62). Enhanced reduction in REM latency in response to the muscarinic agonist arecoline, which has been demonstrated in patients with acute and remitted depression (63), was observed in a preliminary study of patients with borderline personality disorder as well (64), raising the possibility that greater cholinergic responsiveness may also contribute to affective symptoms in affectively unstable personality disorders. In contrast, classic state-dependent correlates of major depressive disorder, such as the dexamethasone suppression test, have failed to consistently distinguish patients with borderline personality disorder from patients with other personality disorders (65).

Hyperresponsiveness of the noradrenergic system also may be associated with affective instability. Patients with borderline personality disorder, particularly those with comorbid schizotypal personality disorder, may demonstrate greater behavioral responses to the catecholamine-releasing agent amphetamine (66). The affective sensitivity and addictive behaviors of "hyster-

oid dysphoric" patients, who are defined by their pronounced emotional reactivity to losses, respond to the monoamine oxidase inhibitors (MAOIs), which serve to stabilize catecholaminergic function (67). In contrast, neuroendocrine and behavioral responses to noradrenergic challenges in major depressive disorder tend to be blunted (58). These results raise the possibility that instability and hyperresponsiveness of catecholamine function, in contrast to the hyporesponsive catecholamine function associated with the classical affective disorders, may contribute to the affective instability of patients with borderline personality disorder. It is unclear to what extent affective instability might occur in attenuated form in other "dramatic cluster" diagnoses; investigation using biological correlates of affective disorders across personality disorders is called for.

Treatment Implications

Agents that stabilize catecholaminergic function and possibly those which antagonize cholinergic function may be helpful for both the discrete depressive episodes as well as the affective instability of the patient with borderline personality disorder. MAOIs such as phenelzine have been demonstrated to be effective for borderline personality disorder (68), for atypical depressive episodes often observed in patients with personality disorders, and for the rejection sensitivity of hysteroid dysphoria (67). The emotional instability of affectively unstable personality disorders has also been reported to be responsive to lithium carbonate (69) and carbamazepine (70), both of which may stabilize neurotransmitter function. Since no mechanism has yet been convincingly established for the affective instability of the personality disorders, more informed pharmacological treatments await further investigation.

Affective lability may have long-term consequences for self-esteem and the capacity to relate to others that are not easily reversed by pharmacological intervention. Psychotherapeutic strategies (71) might permit modification of deeply ingrained, maladaptive interactional patterns, originally developed as strategies to modulate unstable affective states.

ANXIETY/INHIBITION

Definition

Anxiety/inhibition may be defined as the subjective and physiological concomitants of anticipation of future danger or aversive consequences of current behavior, e.g., punishment (7). Pathological anxiety may be based on an excessive sensitivity to punishment. The anxious individual is thus more ready to interpret environmental events as threatening and manifests an excessive reaction to stimuli that others might find relatively innocuous. The reaction to the perceived threatening events is characterized by heightened arousal and a transient inhibition of motor responsiveness. When the anxious individual acts, it is

often in the direction of avoidance of or withdrawal from the environment.

A number of the *DSM-III-R* personality disorders, particularly those of the "anxious" cluster, are characterized by behaviors that may be related to maladaptive attempts to ward off anxiety. For example, in avoidant personality disorder the anxiety associated with the anticipation of rejection is forestalled by avoiding relationships that might culminate in the experience of disappointment. Obsessive-compulsive personality disorder is marked by an excessive need for order to reduce anxiety related to uncertainty regarding future consequences of behavior. Dependent personality disorder is characterized by a pervasive pattern of submissive behavior associated with anxiety regarding initiating activity and fear of disapproval and abandonment. Anxiety regarding the direct expression of anger is considered central to the passive resistance and procrastination of passive-aggressive personality disorder. Individuals with any of these disorders can be viewed as having developed behavioral patterns determined in part by a need to manage exaggerated anxiety responses, although the empirical justification for each of these disorders and their association with an underlying dimension of anxiety/inhibition require further investigation.

Biological Correlates

The "anxious cluster" of personality disorders has perhaps the least well-documented relationship to the axis I anxiety disorders. Family studies have yet to be undertaken in patients with "anxious cluster" personality disorders to determine whether they demonstrate familial aggregation and whether they are familially related to the anxiety disorders. However, biological factors have been implicated in the pathophysiology of anxiety symptoms in the personality disorders. Anxious/inhibited individuals demonstrate higher tonic levels of cortical arousal and sympathetic arousal, lower sedation thresholds, and diminished habituation to novel stimuli (5, 7, 9, 43).

Hypotheses of altered noradrenergic, γ -aminobutyric acid (GABA)-minergic, or chemoreceptor function have been suggested for the axis I disorders but have not yet been actively investigated in the "anxious cluster" disorders.

Clinical Implications

Lacking a specific biology for anxiety-related personality disorders, there can be no specific implications for psychopharmacological intervention, although anti-anxiety medications may aid in the management of the more anxiety-related symptoms of these patients. These patients may be more amenable than impulsive or schizotypal patients with personality disorders to psychodynamic psychotherapy aimed at examination of conflicts underlying defensive behavioral patterns or behavior therapy aimed at reducing overt anxiety.

IMPLICATIONS OF THE DIVISION BETWEEN AXIS I AND AXIS II

There has been a tendency for psychiatrists to regard biological factors as key determinants of the pathogenesis of the axis I disorders and psychosocial developmental factors as key determinants of the pathogenesis of the axis II disorders (65, 72). Both axis I and axis II disorders, however, may represent manifestations of the interaction between the environment and underlying genetic predispositions. Genetic studies of the axis I disorders raise the possibility that corresponding axis I and II disorders may be related along a continuum, as, for example, in the schizophrenia spectrum disorders. Although less evidence exists for anxiety/inhibition, affective, and impulsivity/aggression spectrum disorders, these possibilities invite systematic investigation. Genetic susceptibilities to, for example, cognitive disorganization can be expressed in enduring personality traits that either directly reflect the "core" predisposition (e.g., eccentric appearance, odd speech) or represent adaptations to the "core" vulnerability (e.g., social isolation) to forestall emergence of psychotic symptoms. When these adaptations fail, the genetic vulnerability can be expressed as symptomatic episodes (e.g., a schizophreniform episode) in response to stress, accounting for the high comorbidity of axis I and axis II disorders (65).

This model has an important nosological implication, namely, that although the division between axis I and axis II may be valuable from a clinical point of view, the pathophysiology of psychiatric disorders may transcend this division. Current controversies in the formulation of *DSM-IV* revolve around the appropriate placement of disorders (such as schizotypal personality disorder, dysthymia, and social phobia/avoidant personality disorder) that represent enduring characteristics, compatible with the axis II disorders, but are phenomenologically and biologically linked with their corresponding axis I disorders. These nosological ambiguities may reflect the fact that disorders with a similar underlying pathophysiology may present as axis I and/or axis II conditions. A dimensional or "spectrum" approach that transcends the two axes should be considered when sufficient data are available for future psychiatric diagnostic systems.

IMPLICATIONS OF A DIMENSIONAL APPROACH FOR DEVELOPMENT

A dimensional psychobiological approach to personality may be useful in generating testable hypotheses on the ways innate differences influence the developing child's experience of and strategies to cope with his or her environment. For example, the impulsive child might tend toward action as a response to internal needs or distress, while the anxious/inhibited child will more likely take a cautious approach to initiating activity. The ways in which these strategies are molded into the enduring cop-

ing patterns of adult personality will depend in part on the responses of important caretaking figures. Often parents focus on and identify with characteristics of the child that represent either unwanted vulnerabilities (e.g., impulsivity/aggression, anxiety/inhibition) or strengths (e.g., motor skills, intelligence). The nature of the parents' attributions of and/or identification with the child as a function of both parents' and child's predispositions and defensive styles may be important in determining how the child's vulnerabilities unfold (3, 73).

For example, a mother struggling with her own vulnerability to cognitive disorganization may find it particularly difficult to interact with an infant with impaired psychomotor coordination and may thus experience the child as difficult, while an unusually empathic mother may help to compensate for an underlying neurointegrative impairment. An anxious parent with a strong need to deny or control aggression may react to an active, impulsive infant by excessively constraining the child's activity and labeling the child as destructive or "out of control." In contrast, a more action-oriented parent may indulge the aggressiveness of the developing child, who, if the parent is too permissive, may fail to internalize social norms appropriately. Thus, the ultimate adaptiveness of the adult personality may depend on the "goodness of fit" between the child's predispositions and vulnerabilities and the caretakers' resources and demands.

Individual differences along these dimensions may also influence the way in which the developing child experiences and begins to internally represent his or her environment. By the age of 2 months infants may be able to retain representations of their environment; by 10 months they can react to "mismatches" from expectations of the mother. These prototypical representations form the basis for more differentiated internal representations of self and others that provide the expectational set the individual brings to interpersonal interactions (74). Individual psychobiological differences in intensity and regulation of affects, impulsivity/aggression, anxiety/inhibition, and cognitive/perceptual organization might influence the developing child's mode of representing the world around him or her.

The following examples of the emergence of specific personality traits and defenses associated with the proposed core dimensions are presented to illustrate the utility of the psychobiological perspective for development. These examples are presented in the context of established processes of normal development that may be influenced by variations along each psychobiological dimension. Although some of these considerations are speculative, each generates testable hypotheses that stimulate the investigation of the relationship between the biology underlying these dimensions and personality psychopathology.

Cognitive/Perceptual Organization

What might be the consequences of a vulnerability in the dimension of cognitive/perceptual organization? In

the earliest stages of development, infants must learn to organize their experience and engage caretakers in dyadic relationships (74–76). Their interactions are grounded in rhythmic reciprocal facial expressions, head and body movements, and vocalizations; these become entrained or temporally matched between the mother and the child. Frame-by-frame film analyses of these interactions reveal "interlocking" behaviors between mother and child that are synchronized on the order of fractions of a second (76, 77). This reciprocal engagement appears to form the template for later empathy and interpersonal rapport. The successful mutual engagement of mother and infant depends on the developing child's capacity to screen and respond appropriately to the mother's signals as well as the mother's capacity to attune to the infant's expressive behavior.

An altered capacity to respond smoothly and appropriately to maternal cues grounded in an underlying disturbance in cognitive/perceptual organization could easily impair the development of synchronous, mutually satisfying relationships, as has been documented for preterm infants (77). Impaired information processing and ensuing misrepresentation of the environment might also result in less coherent representations of the environment, less empathy and rapport, and erratically inappropriate or "odd" behavior, as observed in schizoid children and the offspring of schizophrenic parents (31, 78).

Indeed, neurological dysfunction and psychomotor incoordination have been documented to be greater in the high-risk infant offspring of schizophrenic parents, a higher than expected proportion of whom later develop schizotypal personality disorder (79). Attentional abnormalities have also been demonstrated in the offspring of schizophrenic patients and are associated with social detachment (31). The impact of the neurointegrative impairment requires more explicit investigation in longitudinal "high-risk" studies, but these observations suggest that interpersonal as well as cognitive development may be sensitively affected.

Affective Instability

Individual differences in affective responsiveness can be observed in children (8) and have been associated with at least one biological variable—greater adrenocortical responsiveness—in both adults and newborns (80, 81). In primates, marked individual differences in both behavioral and psychobiological reactions to maternal separation that appear to have a substantial genetic component have been demonstrated in longitudinal studies of the rhesus monkey and have been associated with altered adrenocortical and catecholaminergic functioning (82).

How might a propensity for less modulation or instability of affective states influence the process of affective differentiation in the developing child? The progressive differentiation and regulation of affective states is an important concomitant of personality development. Even in beginning infancy, individual differences be-

tween infants can be observed in the discreteness and organization of sleep states (REM and non-REM) and waking states of alert arousal (83). The infant's affective states, signaled by crying, smiling, etc., provide cues to the mother of changes in the infant's internal or external milieu, and their recurrence provides an organizing framework for the interaction between child and caretaker. As the child matures, the regulation and expression of affective states continue to play a major role in shaping interactions with parents.

Affective states may also powerfully color the way in which the world is experienced, encoded internally, and retrieved from memory. Thus, the way in which developing children perceive themselves in relation to others may depend in part on their affective state, analogous to "state-dependent" learning (84). For example, when frustrated and angry, children may perceive themselves and/or their caretakers as bad, while euphoric, excited states may be associated with feelings of omnipotence.

Affectively unstable children might be expected to be more sensitive to transient frustrations and separations throughout their development, thus impairing their mastery of these inevitable concomitants of normal development and distorting their self-image and affective perception of others. They may attempt to avoid the dysphoria of separation by clinging to the mother, interfering with the normal development of autonomy, or attempting to secure her continued presence by displays of distress or "tantrums" that take on a "manipulative" quality. Their appraisal of themselves and others may be powerfully influenced by intense, recurrent dysphoric feelings, so that they may tend to experience themselves in the context of the negative feelings of separation as "defective" and their caretakers as abandoning or frustrating (71). Wide oscillations in affect might impair continuity in the sense of self and others. Highly polarized dissociated affective states may promote "splitting"—the defensive separation of aggressively charged representations from more idealized, positively charged images (85). The underlying affective lability and ensuing alterations in representations of self and others may ultimately manifest themselves as the affective and relational instability of the adult patient with borderline or histrionic personality disorder.

Impulsivity/Aggression

Marked individual differences in aggression that exhibit longitudinal stability are present by the age of 3 (86). Children also show variation along a dimension of reflectiveness versus impulsivity/aggression in their approach to problem solving and their ability to monitor their own behaviors (87), particularly those behaviors which are prohibited.

How might the capacity to inhibit impulsivity/aggression influence growing children's mastery of their motor responses to their environment as well as their evolving experience of self in relation to others? Increased motor activity and aggression in response to frustration in the child may engender anxiety and disapproval in parents,

contributing to a negative self-perception. A relative insensitivity to the prospect of punishment and an associated failure to inhibit aggressive behaviors that result in punishment might also be expected to interfere with the normal internalization of prohibitions against such behaviors. Impairment of the conscience or "superego" would be a likely consequence of the impulsive diathesis that might be expressed as "superego lacunae" (88) (as in the sociopath) or as primitive, harsh forerunners of the mature superego (as in the patient with borderline personality disorder) (85).

Anxiety/Inhibition

Stable, individual differences between children have been clearly documented for the dimension of anxiety/inhibition. Psychobiological correlates of this dimension include the greater sympathetic nervous system activity and adrenocortical responsiveness associated with anxiety disorders. These differences may be detected even in infancy in regulation of heart rate and arousal (9). Offspring of patients with panic disorder and/or agoraphobia are more likely to manifest inhibition than offspring of control subjects (89). Longitudinal studies could be designed to test the hypothesis that these inhibited children will develop personality disorders of the "anxious cluster" with higher than expected frequency.

Mastery of anxiety is required for the child to venture out beyond familiar and comfortable surroundings and explore the environment. How would children with a very low threshold for anxiety meet this challenge? Such children would tend to be shy, inhibited, and fearful and would experience difficulty in forming new relationships or mastering new situations. As a result, they may be more dependent on familiar caretakers and avoid novel situations. They might also be more apprehensive of potential negative consequences of their behaviors and be less able to arrive at action-oriented solutions to interpersonal conflicts or dilemmas. The inhibition could interfere with their learning the more realistic and often beneficial outcomes of more assertive behaviors. Fearful children may be more likely to experience anxiety and inhibition in potentially conflictual situations involving the expression of aggression such as competitive activities with peers. Accordingly, they could tend to develop avoidant, dependent, or compulsive traits as long-term strategies to forestall the dysphoric experience of anxiety.

IMPLICATIONS FOR FUTURE INVESTIGATION

Although this psychobiological dimensional model of personality disorders includes some speculative considerations, such a schema nevertheless suggests a number of useful strategies that might test the following hypotheses.

Hypothesis 1: A dimensional schema cuts across the personality disorders but provides a superior organiz-

ing principle and closer association with external validators than a simple categorical approach. It provides a link between the axis I disorders and their related axis II disorders. This hypothesis could be tested in patients with *DSM-III-R* personality disorders by evaluating specific dimensions of psychopathology; specific external validators such as family history, biological correlates, treatment response, and clinical course; and the relationship of these disorders to the analogous axis I disorders.

Hypothesis 2: Cognitive/perceptual organization is a dimension that spans a continuum from schizophrenia to milder forms of schizoid personality disorder. These disorders are genetically related and characterized by alterations in biological tests of higher cortical organization or information processing. Psychotic-like symptoms are associated with abnormalities in dopaminergic function. These hypotheses can be tested by using both genetic and biological strategies in schizophrenic and schizotypal patients, their relatives, and "high risk" subjects.

Hypothesis 3: Impulsivity/aggression is a genetically transmitted dimension associated with reductions in serotonergic activity. It may be associated with the impulsive personality disorders or the axis I impulse disorders. If this hypothesis is proved correct, family studies should demonstrate a coaggregation of impulsivity/aggression and indexes of reduced serotonergic function. Impulsive/aggressive individuals should show reductions in symptoms with serotonergic agents.

Hypothesis 4: Affective instability is a genetically transmitted dimension that may be related to abnormalities in cholinergic and catecholaminergic function. This hypothesis predicts that patients with personality disorders and their relatives with affective instability will show greater responses to cholinergic and adrenergic challenges.

Hypothesis 5: Anxiety/inhibition is a dimension of personality disorder genetically related to the axis I anxiety disorders. As yet, no biological correlates are clear candidates for abnormalities in this system, but the GABAminergic and noradrenergic systems deserve exploration.

Investigations of these hypotheses will undoubtedly generate more specific hypotheses regarding the relationship of these dimensions to specific constellations of behaviors and defenses and their underlying biological mechanisms. The psychobiological approach, without being reductionistic, may provide a heuristic bridge between observable behavioral and psychological phenomena and the molecular mechanisms that are increasingly implicated as substrates of psychopathology.

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Risk Factors for Homelessness Among Patients Admitted to a State Mental Hospital

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***Objective:** This study measured the overall prevalence of homelessness and tested a priori hypothesized risk factors for homelessness among patients admitted to a state hospital. The risk factors included male gender, age under 40 years, black race, urban residence, schizophrenia-related diagnosis, alcohol abuse, and drug abuse. **Method:** For 377 patients admitted to a New York state mental hospital, the 3-month, 3-year, and lifetime prevalences of homelessness were assessed. The associations between these prevalences and the hypothesized risk factors were measured by relative risks in univariate analyses and by odds ratios derived from a logistic regression in multivariate analyses. **Results:** The 3-month prevalence of homelessness was 19%, the 3-year prevalence was 25%, and the lifetime prevalence was 28%. In univariate analyses, significant associations included drug abuse with 3-month prevalence, 3-year prevalence, and lifetime prevalence; urban residence with 3-year prevalence and lifetime prevalence; and age under 40 years with 3-month prevalence. In the logistic regression analyses, the only significant associations were urban residence with 3-year prevalence and lifetime prevalence. Male gender, black race, alcohol abuse, and schizophrenia-related diagnosis had little or no relation to homelessness. **Conclusions:** The overall prevalence of homelessness in these patients was remarkably high. Several strong risk factors for homelessness in the general population had only a moderate effect or no effect on homelessness in this population. Risk factors for homelessness in psychiatric patients may be somewhat different from those in the general population.*

(Am J Psychiatry 1991; 148:1659-1664)

This article presents findings on the prevalence and risk factors for homelessness among patients admitted to a New York state mental hospital. Although it is evident that rising homelessness has had an especial impact on individuals with psychiatric disorders (1-6), empirical data on the occurrence of homelessness

among mental patients remain minimal. Such data are needed for understanding the causes of homelessness, for planning services, and for appreciating the social circumstances of patients at the present time.

Three valuable reports published in the 1980s concerned the overall prevalence of homelessness in patients admitted to state mental hospitals in Ohio (7), Illinois (8), and Michigan (9). Generalizations from their results are difficult because definitions of homelessness and methods of case finding differed across these studies. Nonetheless, taken together, the results indicate that the prevalence of homelessness is generally higher in urban than in rural areas and that it varies widely by region and by hospital. Prevalence at or shortly before the time of admission to a state mental hospital ranged from as low as 1% in some hospitals to as high as 15% in others.

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Supported in part by a grant from the National Alliance for Research on Schizophrenia and Depression.

The authors thank Anne Lovell, Shlomit Haber, Thalia Sudnick, and Pat Stickney for their participation in the research and Mr. Hal Margosian, Dr. Gerald McCleery, and Ms. Cathy Yarensky for their assistance.

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The closest predecessors in the study of risk factors for homelessness among psychiatric patients are two reports on the correlates of residential instability among psychiatric patients (10, 11). In these studies, homelessness was considered as an extreme of residential instability. In spite of the high quality of these two studies, their results were not consistent (see Discussion).

In this study we sought to clarify, build upon, and extend these earlier studies. We measured prevalence and tested a priori hypothesized risk factors for homelessness among state mental hospital patients. On the basis of the results of studies of homelessness in the general population (4–7, 12), we hypothesized that the prevalence of homelessness among psychiatric patients would be related to the following characteristics: gender (higher prevalence of homelessness among male patients), age group (higher prevalence among patients under age 40), race/ethnicity (higher prevalence among black patients), urban location (higher prevalence among patients in New York City than in suburban counties), diagnosis (higher prevalence among patients with schizophrenia-related disorders), drug abuse (higher prevalence among drug abusers), and alcohol abuse (higher prevalence among alcohol abusers). In a previous report that combined data from this study and two other studies (13), a history of certain disruptive childhood experiences (foster care, group home placement, or running away) was found to be strongly associated with homelessness among these psychiatric patients. Therefore, histories of such disruptive childhood experiences were also included in the analysis to control for the confounding effect of this factor.

METHOD

Rockland Psychiatric Center is a New York state mental hospital that provides long-term inpatient care for patients in two suburban counties, Rockland County and Westchester County, and for patients in the Bronx Municipal Hospital Center in New York City. At the time of the study, Rockland Psychiatric Center was also directly admitting numerous patients from emergency rooms when acute-care hospitals in the two suburban counties and in New York City were filled to capacity.

Five hundred fifty-six patients admitted to Rockland for at least 1 week between September 1988 and April 1989 were eligible for inclusion in the study and were assigned to social workers on a rotating basis. Of these 556 patients, 440 were assigned to social workers who returned a questionnaire on every patient assigned to them. The remaining 116 were assigned to three social workers who returned questionnaires on only 57 of the 116 patients assigned to them. Since in choosing which 57 patients to interview out of a possible 116, these social workers may well have introduced bias, we chose to exclude all 116 in order to maintain a representative sample.

Information in the questionnaires was rejected as in-

complete for 63 (14%) of the 440 patients in the study (e.g., patient floridly psychotic, relative unavailable). Thus, we also excluded these 63 patients and based our report on the data from 377 patients.

Social workers were trained and supervised in the use of the questionnaire in the course of the psychosocial assessments of the patients. The section on homelessness elicited information on the cumulative time during which the subjects were homeless in three overlapping and increasing time periods before the current admission, namely, 3 months, 3 years, and since age 17. Homelessness was defined as sleeping in shelters or public spaces. The patient's location (New York City versus suburban county) was defined according to where the patient was staying at the time of hospital admission. In completing the questionnaire, social workers used all available sources of information (patient, chart, family members) and coded their best judgment as to the correct answer.

In a check on reliability, 17 patients remaining on the admission wards after the end of the study were reinterviewed by a different social worker who was blind to the results of the original interviews. Kappas for rater agreement were 0.88 for the dichotomy ever/never homeless in the 3 months before hospital admission, 0.88 for ever/never homeless in the 3 years before hospital admission, and 1.00 for ever/never homeless since age 17. (On both occasions, the same seven patients were rated as ever homeless since age 17; however, the test and retest interviewers disagreed on the timing of homelessness for one patient.)

Primary *DSM-III-R* diagnoses were obtained from the computerized information system used by New York state hospitals. In this article "diagnosis" refers to the patient's primary diagnosis.

Patients with diagnoses of drug or alcohol abuse or dependence (primary or nonprimary) in the present or a previous admission were considered to have a history of drug or alcohol abuse. The great majority (89%, $N=149$) of those with histories of drug or alcohol abuse had the diagnosis in the present admission.

The 3-month, 3-year, and lifetime prevalences of homelessness were defined, respectively, as the proportion of patients who had been homeless 1 night or more in the 3 months, 3 years, and entire adult life (since age 17) before hospital admission. These are not mutually exclusive outcomes; for instance, homelessness in the 3 months before admission contributes to 3-month prevalence, 3-year prevalence, and lifetime prevalence.

Demographic and diagnostic variables were dichotomized in accordance with the a priori hypotheses we have noted. In univariate analyses, relative risks were used to measure the associations between homelessness and these hypothesized risk factors. (Strictly speaking, these relative risks in this cross-sectional study are "prevalence ratios" [14]). Logistic regression was used for multivariate analyses, since the dependent variable was binary (14). In the logistic regression, a variable representing disruptive childhood experiences (history of foster care, group home placement, or running away)

was included, as we have mentioned. Odds ratios, rather than the logistic regression coefficients from which they are derived, are reported to indicate the relative magnitude of the associations with homelessness. Generally, odds ratios approximate relative risks; for common outcomes, such as homelessness in this population, odds ratios tend to overestimate relative risks.

RESULTS

Demographic and diagnostic data on the 377 patients are shown in table 1. Sixty-three percent were men, 73% were under age 40, just over half were black, and just under half were admitted from New York City. More than half of the patients had schizophrenia-related illnesses (schizophrenia, schizoaffective disorder, schizophreniform disorder); 22% had mood disorders (bipolar disorder, depression, dysthymia, cyclothymia), and 24% had other diagnoses. Forty-five percent had histories of either drug or alcohol abuse.

The 3-month prevalence of homelessness was 19%, the 3-year prevalence was 25%, and the lifetime prevalence was 28%. In demographic and diagnostic subgroups, the 3-month prevalence ranged from 11% to 27%, the 3-year prevalence from 20% to 35%, and the lifetime prevalence from 23% to 38% (table 2). Three-month, 3-year, and lifetime prevalences were about the same for patients admitted directly from emergency rooms (19%, 24%, and 27%, respectively) as for patients transferred from other hospitals (19%, 27%, and 30%) (data not shown).

The relative risks for the hypothesized risk factors were all between 1.0 and 2.0 and were in the hypothesized direction (table 2). For the following associations, the 95% confidence interval for the relative risk did not include 1.0: drug abuse with 3-month prevalence (relative risk=1.8), 3-year prevalence (relative risk=1.7), and lifetime prevalence (relative risk=1.6); urban location with 3-year prevalence (relative risk=1.5) and lifetime prevalence (relative risk=1.4); and age group with 3-month prevalence (relative risk=2.0).

In a logistic regression analysis, the hypothesized risk factors and history of disruptive childhood experiences were included simultaneously in the model. The results are shown in table 3. With ever/never homeless in the 3 months before admission as the dependent variable, none of the hypothesized risk factors was significant at the 0.05 level in two-tailed tests. With ever/never homeless in the 3 years before admission as the dependent variable, only urban location (odds ratio=1.9) was significant at the 0.05 level. With ever/never homeless since age 17 as the dependent variable, only urban location (odds ratio=2.0) was significant at the 0.05 level.

DISCUSSION

Our first finding was the high prevalence of homelessness in this population. Twenty-eight percent of

TABLE 1. Demographic and Diagnostic Characteristics of 377 Patients Admitted to a State Mental Hospital

Variable	N	%
Gender		
Male	239	63
Female	138	37
Age group		
≤29 years	143	38
30–39 years	134	35
≥40 years	100	27
Race/ethnicity		
Black	194	51
White	124	33
Hispanic	52	14
Other	7	2
Location		
New York City	186	49
Westchester County	81	21
Rockland County	105	28
Other	5	1
Diagnosis		
Schizophrenia-related	205	54
Mood disorders	81	22
Other	91	24
Drug abuse history		
Present	123	33
Absent	254	67
Alcohol abuse history		
Present	95	25
Absent	282	75
Type of admission ^a		
Direct	209	55
Indirect	168	45

^aA direct admission is from an emergency room; an indirect admission is from another hospital.

these New York state hospital patients had some experience of homelessness in adult life. Every subgroup had a substantial lifetime prevalence of homelessness, including women (26%), patients from suburban counties (23%), and patients 40 years of age and over (23%). Although these results cannot be generalized to all psychiatric patients or even to all of those in state hospitals, they document a surprisingly high prevalence of homelessness in a sizable and important patient population.

The prevalence rate of 19% for homelessness in the preceding 3 months can be crudely compared with results from the three previous studies of the prevalence of homelessness among patients at the time of admission to state mental hospitals (7–9). The prevalence in these studies was always less than 15% and generally much lower than that. Since these studies were carried out in other states and at an earlier time, the higher prevalence in this study might reflect a high rate of homelessness in the New York region and an increasing rate of homelessness in patients across the country in the 1980s. The higher prevalence in the present study may also be related to more systematic case finding.

The second finding was that three of the hypothesized risk factors showed a trend toward an association with homelessness. Patients in urban locations, patients with histories of drug abuse, and patients under age 40 were at increased risk for homelessness in one or more of the

TABLE 2. Prevalence of Homelessness Among 377 Patients Admitted to a State Mental Hospital

Risk Factor	3-Month Prevalence				3-Year Prevalence				Lifetime Prevalence			
	N	%	Relative Risk	95% Confidence Interval	N	%	Relative Risk	95% Confidence Interval	N	%	Relative Risk	95% Confidence Interval
Gender			1.2	0.8–1.9			1.1	0.8–1.6			1.1	0.8–1.6
Male	48	20			63	26			70	29		
Female	23	17			33	24			36	26		
Age (years)			2.0	1.1–3.6			1.4	0.9–2.1			1.3	0.9–1.9
<40	60	22			76	27			83	30		
≥40	11	11			20	20			23	23		
Race/ethnicity			1.2	0.8–1.8			1.2	0.9–1.7			1.1	0.8–1.5
Black	39	20			54	28			57	29		
Other	32	17			42	23			49	27		
Location			1.4	0.9–2.1			1.5	1.1–2.1			1.4	1.04–2.0
New York City	41	22			57	31			62	33		
Other	30	16			39	20			44	23		
Diagnosis			1.2	0.8–1.9			1.2	0.9–1.7			1.2	0.9–1.7
Schizophrenia-related	42	20			57	28			63	31		
Other	29	17			39	23			43	25		
Drug abuse			1.8	1.2–2.7			1.7	1.2–2.4			1.6	1.2–2.3
Present	33	27			43	35			47	38		
Absent	38	15			53	21			59	23		
Alcohol abuse			1.0	0.6–1.6			1.3	0.9–1.9			1.3	0.96–1.9
Present	18	19			29	31			33	35		
Absent	53	19			67	24			73	26		
Total	71	19			96	25			106	28		

TABLE 3. Associations Between Prevalence of Homelessness and Hypothesized Risk Factors Among 377 Patients Admitted to a State Mental Hospital: Results From a Logistic Regression Analysis

Risk Factor	3-Month Prevalence		3-Year Prevalence		Lifetime Prevalence	
	Odds Ratio	p	Odds Ratio	p	Odds Ratio	p
Gender (male versus female)	1.0	0.98	1.1	0.76	1.1	0.81
Age group (<40 years versus ≥40 years)	1.8	0.13	1.2	0.58	1.1	0.73
Race/ethnicity (black versus other)	0.8	0.34	0.8	0.45	0.7	0.14
Location (New York City versus other)	1.7	0.08	1.9	0.02	2.0	0.01
Diagnosis (schizophrenia-related versus other)	1.3	0.37	1.3	0.27	1.4	0.19
Drug abuse (present versus absent)	1.7	0.10	1.6	0.11	1.6	0.12
Alcohol abuse (present versus absent)	0.8	0.41	1.1	0.64	1.2	0.46
Disruptive childhood experiences (present versus absent)	4.1	<0.001	5.5	<0.001	6.2	<0.001

time periods studied. But the relative risks were not greater than 2.0, and only urban location was statistically significant in multivariate analyses. Some further analyses of these three variables (not shown) are of interest. Urban location showed a coherent “dose-response” relationship: patients from New York City had the highest lifetime prevalence of homelessness (33%), patients from Westchester County, which includes some urban areas, had an intermediate prevalence (27%), and patients from Rockland County, the most suburban county, had the lowest prevalence (20%). Drug abuse had a stronger and significant effect in logistic regression analyses that did not control for disruptive childhood experiences, but this was in part due to its association with childhood experiences: drug abusers constituted 55% (N=32) of the 58 patients with disruptive childhood experiences and 29% (N=91) of the 319 patients without such experiences ($\chi^2=15.9$, $df=1$, $p<0.001$). With respect to age group, 3-month,

3-year, and lifetime prevalences were similar for patients 29 years of age or younger (21%, 28%, 31%, respectively) and those 30–39 years of age (22%, 27%, 28%) and then fell to lower levels for patients 40 years of age or older (11%, 20%, 23%), suggesting that the dichotomy we used to test for age effects (less than 40 years versus 40 years and over) was appropriate.

The third finding was that several risk factors for homelessness in the general population had minimal or no associations with homelessness among these patients. These included gender, race/ethnicity, and alcohol abuse. Psychiatric diagnosis also had no effect, although population studies suggest that persons with schizophrenia are at higher risk for homelessness than persons with other psychiatric disorders (4, 6).

Taken together, the results of this study and previous studies suggest that with the exception of urban location, the associations between our hypothesized risk factors and homelessness are either not very strong or

are not consistently present across patient populations. Two previous studies (10, 11) compared many of these factors in residentially unstable and residentially stable patients. For patients in a San Francisco emergency room (10), residential instability was related only to gender, while for aftercare patients in Massachusetts (11), it was related to gender, age, drug abuse, and alcohol abuse. The only positive finding common to both of these studies—that residential instability was higher in men—was not replicated in a third study (15) that compared the social experience of men and women with schizophrenia.

It is difficult to explain why these variables should be more weakly associated with homelessness in studies of psychiatric patients than in studies of the general population. Perhaps some of the factors that presumably cause variation in risk across subgroups in the general population, such as poverty and weak social support (unmeasured in the present study), are pervasive among these patients and hence show little variability across subgroups. Also, there may have been a weakening of some of the demographic variables as predictors of homelessness in the general population in the late 1980s that was not reflected in the major studies of homelessness carried out a few years earlier. In particular, gender differences may be fewer now than in the past. Homelessness among women has grown at a rapid rate in the New York region; by 1990 the ratio of adult men to women in New York City shelters, including shelters for families, was only about 1.4:1 (New York City Human Resources Administration, adult services shelter statistics, Oct. 24, 1990; press release, Office of the Mayor, New York City, Oct. 30, 1990).

For psychiatric patients, other variables may better indicate differences in vulnerability to homelessness than these demographic and diagnostic variables. In a series of studies on psychiatric patients (13), we found that the risk of homelessness among patients with childhood histories of foster care, group home placement, or running away was about three times that of other patients. Also, variables that were not measured in this study, such as social support and the nature and course of symptoms (16), may predict homelessness in these patients.

Several points should be noted in interpreting the results of this study. First, homelessness that had occurred well in the past was probably underreported by Rockland County patients and their relatives. The majority of the patients who had been homeless at all had been homeless in the 3 months before admission. This might be explained by 1) a higher risk of homelessness when patients are acutely symptomatic, as would be the case before hospital admission, 2) a higher risk of hospital admission when patients are homeless, and 3) better recall of more recent homelessness (which would make even the high lifetime prevalence of 28% a minimum estimate).

Second, a few of the patients who had ever been homeless might have been homeless for only 1 or 2 nights, but most of them had substantial histories of

homelessness. Of the 71 patients who had been homeless in the 3 months before admission, 20 had been homeless for less than 1 week, 12 for 1 week to 1 month, and 39 for more than 1 month. We checked whether the factors associated with short-term homelessness were different from the factors associated with long-term homelessness (results not shown) and found no notable differences.

Third, with regard to the exclusion of 116 patients assigned to three of the social workers (see Method), they were assigned on a rotating basis and bias is unlikely. In fact, the excluded patients and the study sample were highly similar in all risk factors except age (39% of the excluded patients and 27% of the study sample were over 40 years of age). If the study sample had had the same age distribution as the excluded patients, the 3-month prevalence of homelessness would have been 18% instead of 19%.

Fourth, unreliable diagnoses may have attenuated associations between homelessness and schizophrenia-related diagnoses, drug abuse, and alcohol abuse. It seems unlikely that a major effect of schizophrenia or alcohol abuse was missed, as these variables had minimal associations with homelessness. However, drug abuse might have appeared as a somewhat stronger risk factor if there had been more precision in its assessment.

Fifth, the temporal sequence and direction of causality cannot be specified for some of the hypothesized risk factors that showed associations with homelessness. In particular, drug abuse and urban location may be either causes or consequences of homelessness (17, 18).

CONCLUSIONS

Several strong risk factors for homelessness in the general population had only a moderate effect or no effect on homelessness among these patients. Apparently, the risk factors for homelessness among psychiatric patients may be somewhat different from those for the general population. This underscores the need for epidemiologic studies to clarify the risk factors for homelessness specifically among psychiatric patients (18, 19).

The finding that 28% of the patients in this study had some experience of homelessness is a telling statement on the conditions in which large numbers of patients have been living. We agree with a recent comment by H. Richard Lamb that the very existence of this problem "can only be considered incredible in a modern affluent nation" (20). It is our hope that the fundamental causes of homelessness among the mentally ill (1) will be addressed and that this type of study will become unnecessary.

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Childhood Origins of Self-Destructive Behavior

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***Objective:** Clinical reports suggest that many adults who engage in self-destructive behavior have childhood histories of trauma and disrupted parental care. This study explored the relations between childhood trauma, disrupted attachment, and self-destruction, using both historical and prospective data. **Method:** Seventy-four subjects with personality disorders or bipolar II disorder were followed for an average of 4 years and monitored for self-destructive behavior such as suicide attempts, self-injury, and eating disorders. These behaviors were then correlated with independently obtained self-reports of childhood trauma, disruptions of parental care, and dissociative phenomena. **Results:** Histories of childhood sexual and physical abuse were highly significant predictors of self-cutting and suicide attempts. During follow-up, the subjects with the most severe histories of separation and neglect and those with past sexual abuse continued being self-destructive. The nature of the trauma and the subjects' age at the time of the trauma affected the character and the severity of the self-destructive behavior. Cutting was also specifically related to dissociation. **Conclusions:** Childhood trauma contributes to the initiation of self-destructive behavior, but lack of secure attachments helps maintain it. Patients who repetitively attempt suicide or engage in chronic self-cutting are prone to react to current stresses as a return of childhood trauma, neglect, and abandonment. Experiences related to interpersonal safety, anger, and emotional needs may precipitate dissociative episodes and self-destructive behavior.*

(Am J Psychiatry 1991; 148:1665-1671)

It is thought that 7%–10% of psychiatric patients injure themselves deliberately (1), and about 5% of individuals with personality disorders end their lives by suicide (2). The literature has suggested that self-injurious behavior is quite distinct from suicide attempts in intent, lethality, age at onset, sex ratio, and interpersonal meaning (3–6). Deliberate self-harm typically starts in adolescence and involves numerous episodes and a variety of methods, including cutting, burning, slashing, banging, picking, and bone breaking (7, 8). In contrast with self-injury, suicide attempts are reported not to provide relief, to be repeated less frequently, and to have less communicative value (3).

Over the years, a rich clinical literature about self-injurious behavior has evolved that repeatedly mentions

childhood histories of physical or sexual abuse or repeated surgery (3–15). Two prospective studies of abused children recorded self-destructive acts. Green (16) found that 41% of a group of physically and sexually abused children engaged in head banging, biting, burning, and cutting. Rosenthal and Rosenthal (17) found suicidal behavior, self-destructive acts, and decreased sensitivity to pain in 16 children between 2 1/2 and 5 years of age who had been victims of abuse and neglect. Recently, the association between self-destructive behavior and trauma has been enhanced by reports about self-mutilation starting after rape (18) and war trauma (19).

Dissociation is a frequent concomitant of self-injury. Many patients report feeling numb and “dead” prior to harming themselves (3–13, 20). They often claim not to experience pain during self-injury and report a sense of relief afterward (1, 3–14). Episodes of self-mutilation often follow feelings of disappointment or abandonment (4–12).

Research on nonhuman primates has demonstrated that self-mutilation is a common reaction to extreme disruptions of parental caretaking in other mammalian species as well. For example, isolated young rhesus monkeys engage in self-biting and head slapping and banging (21). Analgesia is also common in self-destructive animals.

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Supported in part by NIMH grant MH-34123.

The authors thank Idell Goldenberg, M.A., Beth Hoke, M.A., Chris Pagano, Ph.D., and Barbara Matthews, who served as research assistants.

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Using both historical and prospective data, the present study examined how histories of childhood trauma and disruptions in parental caregiving are related to suicide, self-injurious behavior, eating disorders, and dissociation.

METHOD

The subjects were initially chosen for an ongoing longitudinal study to validate the diagnosis of borderline personality disorder in comparison to antisocial personality disorder, schizotypal personality disorder, and bipolar type II affective disorder. This sample of young adults aged 18–39 years was gathered from clinical settings at Cambridge Hospital, from advertisements in local newspapers, and from the local probation department. Details of the method for subject selection and diagnosis have been reported elsewhere (22–26). Ninety-one subjects entered the study between 1980 and 1981; 33 more subjects were added during a second period, 1985–1986, for a total initial group of 124. Of these subjects, 86 (69%) consented to regular follow-up in the longitudinal study. Most of the initial diagnostic interviews were conducted by the principal investigator of the longitudinal study (J.C.P.). Information about lifetime history of self-destructive ideas and behavior was gathered at intake from all subjects by means of an impulse-anger checklist (23) administered by a research assistant blind to the diagnoses. This included a rating for suicidal ideation and a tabulation of the number of reported suicide attempts, episodes of skin cutting, other self-destructive behavior (such as banging and burning), risk-taking behavior, and eating disorders. Subjects were seen by the research staff approximately every 4–6 months for follow-up interviews. In 1983 a new follow-up measure was introduced that assessed these self-destructive behaviors and impulses on a weekly calendar basis.

From 1986 to 1988 we attempted to contact all subjects in the longitudinal study for further interviews. We were able to trace 76 (88%) of the 86 subjects of the longitudinal study, of whom 74 consented to be interviewed. Two of us (B.A.vdK. and J.L.H.), who were blind to all other previously obtained information, then interviewed these subjects with the Traumatic Antecedents Questionnaire to obtain childhood histories of abuse and disruptions in parental care. The questionnaire is a 100-item semistructured interview that generally takes between 1 and 2 hours to administer. It includes detailed questions about primary caretakers and other important relationships in childhood and adolescence, family discipline and conflict resolution, family alcoholism, domestic violence, and physical and sexual abuse. Details of this questionnaire and of the scoring of childhood trauma have been published previously (25).

Disruptions in parental care were rated in the areas of physical neglect, emotional neglect, family chaos, and significant separations from primary caregivers. Subjects received a positive score for physical neglect if they reported

not having received the most elementary attention with respect to food, shelter, and clothing, such as having to procure their own food or not receiving medical attention for serious physical problems. Emotional neglect was scored on the basis of responses to such questions as “Who did you feel safe with growing up?” “Who was affectionate to you?” and “Who treated you as a special person?” Family chaos was scored on the basis of answers to the questions “Who made the rules and enforced discipline at home?” “What were the rules like?” and “How did your parents solve their disagreements?” The interviewers wrote down the subjects’ stories in response to these questions and then scored them by a consensus rating. Only the most glaring deviations from contemporary norms for parental care (incidents that by law would require reporting to the Department of Social Services) were scored as positive.

The protocols were scored for the occurrence of three types of trauma—physical abuse, sexual abuse, and witnessing domestic violence—and for the four types of disrupted parental care at each of three developmental stages—early childhood (0–6 years), latency (7–12 years), and adolescence (13–18 years). Subjects were also given the Dissociative Experiences Scale (27), which is a self-report measure of experiences with dissociative states.

Data analysis was conducted by means of cross-tabulation and Kendall’s tau computation for ordinal by categorical variables. We used a general linear models procedure for stepwise linear regression, with post hoc analysis for comparison of means for continuous variables. Spearman correlation coefficients were calculated for bivariate relationships. Rating total childhood trauma and disrupted parental care as a continuous variable allowed for correlating the severity of trauma, neglect, chaos, and separations with various forms of self-destructiveness.

RESULTS

Seventy-four subjects, 39 women and 35 men, were given the Traumatic Antecedents Questionnaire. Of these, 24 (32%) met the *DSM-III* criteria for borderline personality disorder and had scores of 28 or higher on the Borderline Personality Disorder Scale (22, 23); 17 (23%) had borderline traits (defined as fulfilling four of the *DSM-III* criteria for borderline personality disorder and scoring higher than 23 but lower than 28 on the Borderline Personality Disorder Scale); 19 (26%) met the *DSM-III* criteria for antisocial personality disorder; 25 (34%) met the criteria for schizotypal personality disorder; and 44 (59%) met the criteria for bipolar II disorder. Because of the prevalence of multiple study diagnoses, these percentages exceed 100%.

Self-Destructiveness

The self-destructiveness of the subjects is summarized in table 1. Intake data were available for only 70 of the

subjects because four subjects dropped out before completing cross-sectional measures but returned for follow-up interviews. Thus, a total of 74 subjects were available for the duration of the longitudinal study for interviews several times a year (mean=4 years, range=2–9 years). At intake 61 (87%) of the 70 subjects reported histories of some form of self-destructive behavior: 39 (56%) had made one or more serious suicide attempts, 20 (29%) reported five or more episodes of self-inflicted injuries, eight (11%) had cut themselves once or twice, and about half reported histories of binge eating and/or anorexia. During follow-up, some form of self-destructive behavior persisted in 17 (23%) of the 74 subjects: five (7%) made one or two serious suicide attempts, another five (7%) made more than three attempts, and six (8%) engaged in chronic cutting (five or more episodes), of whom three also made one or more serious suicide attempts.

Self-destructiveness and diagnosis. In keeping with the criteria set forth by *DSM-III* and the scores on the Borderline Personality Disorder Scale, borderline personality pathology was significantly associated with suicide attempts ($r_s=0.28$, $N=70$, $p=0.02$), cutting ($r_s=0.38$, $N=70$, $p<0.001$), and other self-injurious behavior ($r_s=0.28$, $N=70$, $p=0.02$). Antisocial, schizotypal, and narcissistic personality disorders and bipolar II disorder were not significantly related to any of the self-destructive behavior.

Self-destructiveness and childhood trauma. Of the 39 subjects who had made suicide attempts, 30 (77%) reported histories of major childhood trauma and 28 (72%) reported disruptions in parental care; five (13%) denied childhood trauma or disruptions in parental care. Of the 28 subjects who reported self-cutting at entry into the study, 22 (79%) gave histories of significant childhood trauma and 25 (89%) reported major disruptions in parental care; only one did not give a history of either childhood trauma or disrupted care. Table 2 displays the Spearman correlations between the magnitude of various childhood trauma scores and quantitative assessment of suicide attempts and self-injurious behavior at intake. Childhood trauma scores were not related to suicidal ideation but predicted suicide attempts, cutting, other self-injurious behavior, and anorexia. Of the three types of trauma, sexual abuse was most strongly related to all forms of self-destructive behavior. Witnessing domestic violence was associated with suicide attempts but not with self-cutting or other self-injurious behavior.

Table 3 shows that the age at which trauma occurs plays a role in both the severity and expression of self-destructive behavior: the earlier the trauma, the more cutting. Abuse during early childhood and latency was strongly correlated with suicide attempts and total self-injurious behavior, while abuse in adolescence was significantly associated only with suicide attempts and anorexia.

Data on self-destructive behavior over the course of the study are summarized in table 4. Histories of sexual abuse, in particular, predicted continued suicide at-

TABLE 1. Self-Destructiveness in Subjects With Personality Disorders or Bipolar II Disorder

Self-Destructive Behavior	Intake (N=70)		Follow-Up (N=74)	
	N	%	N	%
Suicide attempts	39	56	12	16
Cutting	28	40	9	12
Other self-injurious behavior (head banging, picking, or burning)	27	39	12	16
Suicide attempts plus self- mutilation	21	30	10	14
Binge eating	34	49	37	50
Anorexia	32	46	21	28
Risk taking	63	90	34	46

tempts and cutting but not other self-injurious behavior. Chronic cutting during follow-up was associated with trauma at any age (early childhood, $r_s=0.32$, $N=74$, $p<0.001$; latency, $r_s=0.25$, $N=74$, $p<0.05$; adolescence, $r_s=0.24$, $N=74$, $p<0.05$).

Neglect, Separation, and Chaos

We next compared the subjects' reports of separations from parents, environmental chaos, and physical and emotional neglect with self-destructive behavior. These disruptions of attachment were significantly associated with cutting but not with suicide attempts or other self-injurious behavior. Tables 2 and 3 show that both parental neglect and intrafamilial chaos were associated with histories of self-cutting at intake. Table 4 shows the associations between childhood physical and emotional neglect and various forms of self-destructive behavior over the course of the follow-up. Total neglect scores predicted continued suicide attempts, cutting, and other self-injurious behavior. Prolonged separation from caregivers was also related to continued cutting as well as to other forms of self-injurious behavior.

Dissociation

Familiarity with dissociative experiences, as measured by the Dissociative Experiences Scale, was highly correlated with histories of trauma ($r_s=0.38$, $N=74$, $p<0.001$) and histories of neglect ($r_s=0.43$, $N=74$, $p<0.0001$). The dissociation score was also significantly associated with intake histories of cutting ($r_s=0.28$, $N=70$, $p=0.02$) and anorexia ($r_s=0.24$, $N=70$, $p<0.05$), and there was a trend toward a correlation with suicide attempts ($r_s=0.22$, $N=70$, $p<0.10$). During follow-up, the Dissociative Experiences Scale score continued to predict cutting ($r_s=0.35$, $N=74$, $p=0.003$) and suicide attempts ($r_s=0.25$, $N=74$, $p<0.05$).

Interrelations

To determine which childhood variables (trauma, neglect, chaos, and separations) were the most powerful predictors of suicide attempts, cutting, and other self-

TABLE 2. Spearman Correlation Coefficients Between Childhood Trauma/Disruption in Care and Self-Destructive Behavior at Intake for 70 Subjects With Personality Disorders or Bipolar II Disorder

Trauma/Disruption	Suicidal Ideation	Suicide Attempts	Cutting	Other Self-Injurious Behavior	Total Self-Injurious Behavior	Binge Eating	Anorexia
Physical abuse	0.07	0.31 ^a	0.30 ^a	0.25 ^b	0.32 ^a	0.19	0.21 ^c
Sexual abuse	-0.01	0.41 ^d	0.49 ^e	0.16	0.36 ^a	-0.01	0.32 ^a
Witnessing violence	0.04	0.26 ^b	0.07	0.08	0.10	0.21 ^c	0.04
Neglect	0.12	0.19	0.36 ^a	0.08	0.27 ^a	0.01	0.16
Chaos	0.04	0.03	0.27 ^b	0.18	0.34 ^a	-0.01	0.21
Separations	0.07	0.07	0.20	0.06	0.15	-0.01	0.06

^ap<0.01.^bp<0.05.^cp<0.10.^dp<0.001.^ep<0.0001.**TABLE 3. Spearman Correlation Coefficients Between Age at Childhood Trauma/Disruption in Care and Self-Destructive Behavior at Intake for 70 Subjects With Personality Disorders or Bipolar II Disorder**

Age at Trauma/Disruption	Suicidal Ideation	Suicide Attempts	Cutting	Other Self-Injurious Behavior	Total Self-Injurious Behavior	Binge Eating	Anorexia
Trauma							
Early childhood	0.13	0.37 ^a	0.41 ^b	0.16	0.31 ^a	0.21 ^c	0.14
Latency	0.01	0.41 ^b	0.35 ^a	0.13	0.29 ^a	0.02	0.18
Adolescence	0.02	0.33 ^a	0.21 ^c	0.11	0.17	0.12	0.23 ^d
Disrupted care							
Early childhood	0.14	0.16	0.36 ^a	0.06	0.24 ^d	-0.01	0.18
Latency	0.07	0.09	0.41 ^b	0.17	0.34 ^a	-0.10	0.14
Adolescence	0.16	0.10	0.31 ^a	0.20 ^c	0.34 ^a	-0.06	0.18

^ap<0.01.^bp<0.001.^cp<0.10.^dp<0.05.**TABLE 4. Spearman Correlation Coefficients Between Childhood Trauma/Disruption in Care and Continued Self-Destructive Behavior During Follow-Up for 74 Subjects With Personality Disorders or Bipolar II Disorder**

Trauma/Disruption	Suicide Attempts	Cutting	Other Self-Injurious Behavior	Total Self-Injurious Behavior	Binge Eating	Anorexia
Physical abuse	0.06	0.20 ^a	0.07	0.18	0.24 ^b	0.05
Sexual abuse	0.31 ^c	0.30 ^c	0.19	0.26 ^b	0.01	0.02
Witnessing violence	0.14	0.17	0.14	0.12	0.08	0.08
Neglect	0.33 ^c	0.40 ^d	0.35 ^c	0.40 ^d	0.04	0.19
Chaos	0.11	0.22 ^a	0.02	0.14	0.14	0.10
Separations	0.14	0.23 ^b	0.33 ^c	0.35 ^c	-0.03	0.02

^ap<0.10.^bp<0.05.^cp<0.01.^dp<0.001.

injurious behavior, we conducted a series of six stepwise regression analyses (table 5). Lifetime history data obtained at intake were examined separately from data obtained during the course of follow-up, which reflect prospectively observed behaviors. Childhood neglect and trauma together significantly predicted cutting at intake for a total of 20.8% of the variance reported. Childhood trauma predicted 19.2% of the variance for suicide attempts at intake and 4.5% of the variance for other self-destructive behavior. The follow-up data re-

vealed that childhood neglect predicted 12.3% of the variance for suicide attempts, childhood neglect and separations predicted 18.4% of the variance for cutting, and separations and neglect predicted 24.1% of the variance for other self-destructive behavior.

To test the hypothesis that dissociation, as measured by the Dissociative Experiences Scale, adds to the capacity to predict self-injurious behavior (after controlling for empirically related childhood variables), we repeated the analyses in table 5 using hierarchical regressions. The

TABLE 5. Stepwise Regression Analyses of Childhood Variables Predicting Adult Suicidal and Self-Injurious Behavior

Outcome Variable	Childhood Variable	F	df	p	R ²	Total R ²
History at intake						
1. Suicide attempts	Trauma	16.12	1, 68	0.002	0.192	0.208
2. Cutting	Neglect	12.69	2, 67	0.007	0.157	
	Trauma	4.33	2, 67	0.04	0.051	
3. Other self-injurious behavior	Trauma	3.23	1, 68	0.08	0.045	
Behavior during follow-up						
1. Suicide attempts	Neglect	10.09	1, 72	0.002	0.123	0.184
2. Cutting	Neglect	12.39	2, 71	0.0008	0.147	
	Separations	3.19	2, 71	0.08	0.037	
3. Other self-injurious behavior	Separations	16.53	1, 72	0.0001	0.187	0.241
	Neglect	5.05	1, 72	0.03	0.54	

TABLE 6. Hierarchical Regression Models Testing the Effect of Adding Dissociation to Childhood Variables Predicting Cutting and Other Self-Injurious Behavior

Factor	Independent Variable	F	df	p	Total R ²
History of cutting at intake	Neglect	13.07	3, 64	0.0006	0.241
	Trauma	4.48	3, 64	0.04	
	Dissociation	2.79	3, 64	0.10	
Cutting during follow-up	Neglect	12.92	3, 68	0.0006	0.242
	Separations	3.30	3, 68	0.07	
	Dissociation	5.51	3, 68	0.02	
History of other self-injurious behavior at intake	Trauma	3.48	2, 67	0.07	0.059
	Dissociation	0.64	2, 67	0.43	
Other self-injurious behavior during follow-up	Separation	16.32	3, 68	0.0001	0.238
	Neglect	4.82	3, 68	0.03	
	Dissociation	0.05	3, 68	0.82	

childhood variables with alphas less than 0.10 were entered in order, and the Dissociative Experiences Scale score was entered last. The Dissociative Experiences Scale score added no significant variance in predicting suicide attempts at intake or at follow-up (data not shown). However, table 6 shows that dissociation contributed to prediction of cutting but not of other self-injurious behavior. For the intake data, adding the Dissociative Experiences Scale score after neglect and trauma yielded a nearly significant trend toward predicting 24.1% of the variance. For the follow-up data, adding the Dissociative Experiences Scale score after neglect and separations significantly improved the model, predicting 24.2% of the cutting but not other self-destructive behavior observed during follow-up.

DISCUSSION

These findings demonstrate that histories of childhood physical and sexual abuse, as well as parental neglect and separations, are strongly correlated with a variety of self-destructive behavior in adulthood, including suicide attempts and cutting. Unlike previous reports, we found only a moderate association with eating disorders, which may be a function of the pervasiveness of binge eating and anorexia in our total sample and of the narrow definitions of trauma and neglect used in this study. Suicidal ideation was not related to either trauma or neglect.

During the follow-up phase of the study, our subjects were regularly seen by the study staff. In addition, approximately half of them were in therapy most of the time and the rest a substantial proportion of the time. During this period, only the subjects who reported histories of sexual abuse and those with the most severe histories of separation and neglect tenaciously continued to engage in self-destructive activities. At intake, histories of parental neglect had predicted cutting but not suicide attempts; however, during the course of the study, neglect became the most powerful predictor of self-destructive behavior. This implies that although childhood trauma contributes heavily to the initiation of self-destructive behavior, lack of secure attachments maintains it. The subjects who had experienced prolonged separations from their primary caregivers, and those who could not remember feeling special or loved by anyone as children, were least able to utilize interpersonal resources during the course of the study to control their self-destructive behavior.

The analysis of the role of dissociation in self-destructive behavior suggests that cutting differs from other methods of self-injury and from suicide attempts. Our findings indicate that ongoing dissociation is directly associated with cutting. As previously described (4–8, 12, 20, 28, 29), although dissociation provides protective detachment from overwhelming affects, it also results in a subjective sense of deadness, of disconnection from others, and of internal disintegration. While many persons who cut themselves report that self-mutilation

allows them to terminate this dysphoric state of mind, for a minority self-injury is not accompanied by depersonalization or analgesia (8, 30, 31).

Suicide attempts, cutting, and other self-injurious behavior may serve different functions in regulating affective states. They may be active attempts to kill, injure, or quiet menacing hallucinations, as well as ways to manage unbearable affects by altering interpersonal conditions and the biological homeostasis (32–34). Our findings that suicide attempts were most strongly associated with childhood trauma, cutting with neglect, and other self-injurious behavior with separations need to be replicated in larger samples to define more clearly the meaning, function, and effects of these various self-destructive actions. Our data suggest that trauma-related interpersonal communications play a significant role in suicide attempts, while cutting primarily serves to regulate internal affective states.

Clinically, patients and therapists attribute a variety of meanings to these behaviors, which is understandable in light of the range of early emotional injuries related to physical self-destructiveness. Thus, they may be experienced subjectively as self-punishment, as a way of punishing others, or as a cry for help after feeling abandoned.

The fact that both the severity of the trauma and the age at which it occurred affected the particular ways in which our subjects were self-destructive suggests that both psychological and biological maturity play a role in how experiences of abuse and neglect are managed. Recent studies indicate that disruptions in early caregiving may have long-term consequences for biological self-regulating systems. Thus, abuse and neglect may impair both the capacity for self-regulation of affective states and the ability to utilize interpersonal relations for affect regulation (33–35).

In a 1974 study of self-mutilation among violent male prisoners, Bach-y-Rita (13) concluded, "The syndrome of withdrawal, hyperarousal, depression, impaired pain perception and violent aggressive reactions against self and others is so consistent, that it is most likely biologically based, and the consequence of having been reared under conditions of social deprivation or repeated terror. This constellation of symptoms is commonly seen amongst socially deprived young animals as well." Since then, research on nonhuman primates has amply demonstrated that self-mutilation is a common reaction to social isolation and fear (36, 37). In animals, environmental cues associated with previous exposure to noxious stimuli continue to precipitate conditioned biological emergency responses over time, resulting in freeze, fight, or flight reactions. Immature animals are particularly vulnerable to developing such conditioned emergency responses to repeated stress and to previously neutral events associated with the noxious stimulus (38, 39).

Survivors of severe trauma have repeatedly been described as continuing to react with extremes of under- and overarousal to even minor emotional stressors. They seem to keep responding to stimuli reminiscent of

the trauma with conditioned psychological and biological stress responses that do not extinguish over time (12, 33, 40, 41). Many self-destructive people follow these patterns; they may experience intense physiological disorganization in the face of minor stress, giving rise either to impulsive and aggressive actions or to the triad of dissociative reactions, psychic numbing, and physical analgesia (5–13, 20, 28). It is likely that the immaturity of the CNS of children makes them more vulnerable than adults to developing lasting biological changes in response to trauma and neglect. However, we recently demonstrated that even adults with post-traumatic stress disorder develop significant opioid-mediated, stress-induced analgesia when exposed, nearly two decades later, to a trauma-related stimulus (28, 42). There is mounting evidence that the stress hormones which are released when traumatized individuals are reexposed to stimuli reminiscent of earlier traumas play a role in altering their state of consciousness (20, 33, 43). Dissociation, self-destructiveness, and impulsive behavior may all prove to be hormonally mediated responses that are triggered by reminders of earlier trauma and abandonment.

CONCLUSIONS

The findings of this study suggest that therapists treating patients who repetitively attempt suicide or engage in chronic self-injurious behavior need to be prepared to deal with issues of childhood trauma, neglect, and abandonment, both in the past and as reexperienced in current relationships. Our previous work has shown that self-destructive behavior was highly correlated with two psychological conflicts, one centering on separation-abandonment and the other on experiencing and expressing anger and emotional needs (23). When treating self-destructive patients, the therapist must anticipate that painful affects related to interpersonal safety, anger, and emotional needs may give rise to dissociative episodes and impulsive behavior which may be accompanied by increased self-destructiveness. The work of therapy must clarify how current stresses are experienced as a return of past traumas and small disruptions in present relationships as repetitions of prior abandonment. We have written elsewhere (44, 45) about the importance of validation, support, and avoidance of participation in reenactment of the trauma as features of this treatment.

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Reliability of the Part II Board Certification Examination in Psychiatry: Interexaminer Consistency

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***Objective:** The aim of the study was to examine the reliability (interexaminer consistency) of the American Board of Psychiatry and Neurology (ABPN) Part II (oral) examination in psychiatry. **Method:** Grades were assigned independently by two examiners who observed the same examination in a 1-year cycle (1,422 candidates, two examinations each). The consistency between these pairs of grades (pass, condition, fail) was analyzed using a weighted kappa statistic. **Results:** There was perfect agreement between examiners in 67% of examinations, minor disagreement in 26%, and major disagreement in 7% (weighted kappa=0.54–0.56). **Conclusions:** The Part II ABPN examination demonstrates fair to good reliability as measured by interexaminer consistency. Development of more explicit grading criteria should further improve examiner agreement in future examinations.*

(Am J Psychiatry 1991; 148:1672–1674)

Medical specialty certification began in 1917 with the incorporation of the American Board of Ophthalmology, and currently there are 23 such organizations recognized by the American Board of Medical Specialties (1). These boards were created by internal professional forces in order to distinguish those physicians with specialty training from general practitioners. In recent years, however, board certification has also been driven by external forces—public concern that physicians be judged qualified to practice their specialty.

Specialty boards such as the American Board of Psychiatry and Neurology, Inc. (ABPN), have attempted to clearly articulate what they are examining for, that is, what distinguishes more qualified from less qualified specialists. Board certification in psychiatry consists of a Part I (written) examination and a Part II (oral) examination that assesses clinical skills, including the ability to interview a patient; organize and present data; discuss phenomenology, diagnosis, and prognosis; and review etiologic, pathogenic, and therapeutic issues. While 14 of the other specialty boards also require a

written and an oral examination, the ABPN is the only board that still uses “live” patients.

While oral examinations have a long history in educational testing and medical certification, they are usually resource intensive, and questions are often raised about their validity and reliability. With regard to validity, the primary concern is the relatively limited sampling of examinee behavior that this method usually allows compared to multiple-choice questions. In the current psychiatry Part II (oral) examination, candidates are exposed to two cases that can represent only a small segment of psychiatric diagnoses. However, because the emphasis is on the process of the candidates’ thinking about diagnosis and treatment, standardized case content is not considered critical to examination validity.

Perhaps the most pressing concern is lack of adequate data about reliability, or reproducibility, of test scores caused by variation in examiner grading behavior. Critics of the Part II examination, including failing candidates who appeal their grades, have consistently raised the issue of examiner subjectivity (2). Nevertheless, in their review of oral examinations, Muzzin and Hart (3) supported the hypothesis that oral examinations are reliable, concluding that “reasonable reliability has been demonstrated with structured, standardized orals using hand-picked examiners.” Oral examinations continue to be used because they appear to measure significant components of clinical skill not assessed by other test formats. This consideration is particularly compelling in the field of psychiatry, in which physician/patient interaction is a key aspect of clinical competence. As Talbott (4) stated, “Psychiatrists, first and foremost, deal

Received Jan. 30, 1991; revision received May 22, 1991; accepted June 14, 1991. From the Research and Development Committee of the American Board of Psychiatry and Neurology, Inc. (ABPN). Drs. McDermott and McCurdy are Emeritus Directors of the ABPN; Drs. Tanguay, Shore, Tucker, and Terr are Directors; Dr. Scheiber is Executive Vice President; and Dr. Juul is Research Coordinator. Address reprint requests to Dr. McDermott, Department of Psychiatry, University of Hawaii at Manoa, 1319 Punahou St., Honolulu, HI 96826.

The authors thank John Lloyd, Ph.D., and Donald Langsley, M.D., for their assistance in carrying out the study.

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interpersonally with patients, and the ability to relate to psychiatric patients may be the most critical skill they need, one whose absence should perhaps be the only automatic disqualification for Board certification."

This report presents the results of a systematic study of the interrater reliability of the Part II Board certification examination in psychiatry. The study was initiated by the ABPN Research and Development Committee.

EXAMINATION HISTORY

The first attempts to study reliability were carried out by the ABPN Committee on Certification in Child Psychiatry, which administers a subspecialty certification examination to those who have been certified in psychiatry and have additional training in child psychiatry (5). The oral examination was studied over a 2-year period, and it was found that two of the six components were significantly less reliable across administrations. Because they tested knowledge rather than clinical skill, it was decided to convert them to a multiple-choice format so that the same questions were asked of all candidates. Furthermore, new case materials (videotaped cases and written vignettes) were developed to increase the standardization of the four remaining oral examinations.

Meanwhile, the examination in general psychiatry had already been divided into a written Part I (knowledge) and an oral Part II (clinical) examination, the latter requiring that candidates interview two patients with a psychiatric diagnosis. In the 1970s, one of the patient interviews was replaced with a videotape of a psychiatric interview in order to provide more standardization, and a study of the concordance between performance on the two formats was carried out (4, 6). Over half of the candidates studied received identical grades (pass, condition, or fail) on the two formats, similar to concordance rates for other specialty board examinations (7, 8). When there were discrepancies, more candidates did better on the audiovisual examination than on the patient interview. Talbott (4) and Langsley (6) pointed out that differences between the formats are not unexpected because the patient interview allows for assessment of certain skills (e.g., ability to relate to patients, asking appropriate questions) that the videotaped interview does not. This is probably what makes the patient examination more difficult.

METHOD

The sample consisted of the 1,422 candidates who took the Part II oral examination in three different administrations during a 1-year cycle (examinations 1, 2, and 3). The usual examination procedure was followed. For each candidate, the examination consisted of a standard format of two 1-hour sessions. One was a 30-minute interview of a patient with a psychiatric diagnosis followed by a 30-minute discussion of the patient with two examiners who observed the interview. The

other session began with the viewing of a 30-minute videotaped psychiatric interview followed by a 30-minute discussion of the case with a different pair of examiners. In addition to the two primary examiners, a senior examiner supervised two or three examination rooms to monitor the examiners' performance as well as that of the candidates. Data from a complete 1-year cycle of three examination administrations were used, which represented 1,422 candidates or 2,844 individual examinations (two per candidate).

The examiners were Board-certified psychiatrists drawn from a national pool of examiners. Most had served as examiners previously; if an examiner was new or relatively inexperienced, he or she was paired with a more experienced examiner. All examiners participated in a training session the day before the test started in which the purposes and format of the examination, as well as the criteria for assigning grades, were reviewed. The grading categories were pass, condition, or fail. The condition category was assigned when candidates were neither clearly passing nor clearly failing.

For the purpose of this study, the primary examiners were instructed to record independently an initial grade for the candidate. Once the initial grades were recorded, the two primary examiners discussed the candidate's performance and reached a final consensus grade, which was recorded as the official grade for that examination. There was no change in the role of the senior examiners who supervised the process.

The kappa statistic (9, 10) was used to indicate the amount of interrater agreement. Compared to simple rate of agreement between judges, the kappa statistic takes into account the agreement that would be expected by chance alone. With unweighted kappa, all disagreements are equally weighted, whereas weighted kappa allows for degrees of disagreement. Because a pass/fail disagreement was considered to be more serious than a pass/condition or fail/condition disagreement, weighted kappa was used.

For weighted kappa, the cells that represent perfect agreement between examiners (pass/pass, condition/condition, fail/fail) receive the maximum weight of 1. The remaining cells are assigned weights on the basis of expert judgment about the seriousness of the disagreement (11). For this study, disagreements between adjoining categories (pass/condition and fail/condition) were weighted 0.75, while the pass/fail disagreement was weighted 0.

RESULTS

Tables 1 and 2 show the rate of agreement between examiner pairs for the three examinations (examinations 1-3) administered in a 1-year cycle and collapsed across examinations. Across all three examinations, both examiners gave the candidate the same initial grade in 67% (N=1,900) of the examinations. In 16% (N=451) of the examinations they had a pass/condition disagreement, and in 10% (N=280) they had a fail/condition disagreement, for a total of 26% (N=731) minor disagreements.

TABLE 1. Initial Grades Given by Two Examiners to Physicians Who Took Three ABPN Part II (Oral) Examinations

Examination and Examiner 2 Grade	N	Examiner 1 Grade					
		Pass		Condition		Fail	
		N	%	N	%	N	%
Examination 1	600						
Pass		284	47	59	10	23	4
Condition		45	8	44	7	36	6
Fail		15	3	32	5	62	10
Examination 2	688						
Pass		318	46	51	7	24	3
Condition		58	8	57	8	33	5
Fail		33	5	31	5	83	12
Examination 3	1,554						
Pass		780	50	120	8	52	3
Condition		118	8	110	7	68	4
Fail		64	4	80	5	162	10
Total	2,842						
Pass		1,382	49	230	8	99	3
Condition		221	8	211	7	137	5
Fail		112	4	143	5	307	11

They had a major disagreement (pass/fail) in 7% (N=211) of the examinations. Table 2 contains the weighted kappas, which ranged from 0.54 to 0.56, indicating fair to good agreement beyond chance (11). In clinical psychiatric research, agreement between experts has typically been found to fall in the range 0.50–0.59 (12).

DISCUSSION AND CONCLUSIONS

What are the issues to be considered by this level of agreement? For two-thirds of the oral examinations, there was perfect initial agreement between examiners on grades before any discussion of their observations of candidate performance. In one quarter of the cases, the initial disagreement was a one-level or minor one (pass/condition or fail/condition). It would appear that this type of disagreement, which is relatively easily resolved by examiners, can be expected with a significant number of candidates and results when performance is neither outstanding nor grossly deficient. This confirms the findings of the American Board of Pediatrics that marginal candidates are the most difficult to judge consistently in oral examinations (13) and others who have found that borderline candidates are the most likely to suffer from the variability of ratings (14).

The two-level major (pass/fail) disagreement that occurred in 7% of the examinations should be the focus of efforts to further improve the reliability of the Part II examination. Here, even though the examiners resolved the disagreement and reached consensus on a final grade, they were split on their initial impression, which suggests that they may have emphasized different aspects of behavior in their individual assessments of the same candidate.

These data suggest that more explicit grading criteria and more extensive rater training should further improve test reliability. Efforts to further standardize grading criteria have been undertaken. In addition,

TABLE 2. Interrater Agreement of Grades Given by Two Examiners to Physicians Who Took Three ABPN Part II (Oral) Examinations

Examination	Rate of Agreement	Weighted Kappa
1	0.64	0.54
2	0.66	0.55
3	0.67	0.54
Total	0.67	0.56

other innovative methods may be considered in the effort to improve examination consistency. For example, one could consider assigning weights for difficulty of the patients themselves, e.g., on a scale of cooperativeness, in obtaining a psychiatric history.

This study of a 1-year cycle of the Part II certification examination in psychiatry revealed fair to good agreement beyond chance between examiners who independently rated the same candidate's performance. In order to further improve the reliability of its examination, the ABPN has undertaken development of more specific and standardized indicators of performance (explicit criteria for examiner judgments) and examiner training devoted to practice with applying these criteria. Such efforts should result in an even more standardized Board certification examination while retaining the unique patient assessment component of Board certification in psychiatry.

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Abnormal Caloric Requirements for Weight Maintenance in Patients With Anorexia and Bulimia Nervosa

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Objective: This study tested previous findings that patients with eating disorders who attain normal weight have abnormal caloric requirements for maintaining weight. **Method:** Fifty-three female patients meeting the DSM-III-R criteria for anorexia nervosa and/or bulimia nervosa were divided into four subgroups, and their daily caloric intake was measured over a weight-stable period. Patients with anorexia nervosa (restricting and bulimic subtypes) were studied 4 weeks after refeeding and weight gain, when they had attained 95% of average body weight. Patients with normal-weight bulimia (previously anorexic or never previously anorexic) were studied 1–4 weeks after admission to an inpatient unit. **Results:** After weight restoration, restricting anorexic patients required significantly more calories per day to maintain weight than did bulimic anorexic patients, as measured with corrections for weight, body surface area, and fat-free mass. Previously anorexic normal-weight bulimic patients required significantly more calories per day to maintain weight than never-anorexic normal-weight bulimic patients, as measured with correction for weight but not with the other factors used to correct caloric intake. **Conclusions:** To maintain stable weight after weight restoration, restricting anorexic patients require a significantly higher caloric intake than do bulimic anorexic patients. Differences in caloric needs between normal-weight bulimic patients with and without histories of anorexia may depend on the methods used to correct caloric requirements. Body surface area may be the most precise correction factor across different subgroups of eating disorder patients. Elevated caloric requirements, when coupled with reduced food intake, may particularly contribute to relapse in anorexic patients.

(Am J Psychiatry 1991; 148:1675–1682)

The eating disorders anorexia nervosa and bulimia nervosa are associated with considerable morbidity and mortality, partly because a substantial number of patients with these disorders relapse after treatment (1–3). The psychophysiological processes contributing to poor treatment outcome are not well understood. Recent studies at several institutions (4–6) suggest that alterations in caloric utilization, and perhaps energy balance, may tend to perpetuate these disorders and make recovery more difficult.

It is important, first, to recognize that there are several distinct subgroups of patients with eating disorders. Boundaries between subgroups and the terminology used to differentiate these subgroups have been in flux. Nevertheless, a considerable body of literature (7–12) suggests

that certain factors distinguish subgroups of patients with eating disorders. These factors include the amount of weight lost, the type of pathological eating behavior, and certain psychopathological characteristics (13).

The most common eating disorder is bulimia nervosa (DSM-III-R). This disorder is at least 10 times more prevalent than anorexia nervosa (14–16). Bulimic patients periodically binge and purge, usually by vomiting. The majority of patients with bulimia nervosa remain at normal weight (normal-weight bulimia), i.e., they maintain a body weight above 85% of average body weight and have never been emaciated (12, 17, 18). A second subgroup of patients with bulimia nervosa are those who have met criteria for anorexia nervosa either before or after the onset of their bulimic behavior.

Perhaps the best-known eating disorder is anorexia nervosa, of which the most distinguishing characteristic is severe emaciation. Two types of food consumption are seen in anorexia nervosa. Patients who fulfill only the DSM-III-R criteria for anorexia nervosa lose weight exclusively by fasting or restricting food intake. Patients with anorexia nervosa who also binge and/or purge

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(bulimic anorexic patients) qualify for *DSM-III-R* diagnoses of both anorexia nervosa and bulimia nervosa. Compared to restricting anorexic patients, bulimic anorexic patients exhibit more evidence of premorbid behavioral instability, a higher incidence of premorbid and familial obesity, a greater susceptibility to depression, and a higher incidence of behavior suggestive of impulse disorder (7–9, 11). In fact, bulimic anorexic patients appear to share many features in common with normal-weight bulimic patients, for example, impulsive behavior and a predisposition to obesity (12).

Outcome studies have suggested that a considerable number of patients with eating disorders relapse after treatment (1–3). Although this poor outcome has been attributed to psychological and psychosocial factors (19–21), physiological factors (such as abnormalities in caloric requirements for weight maintenance) may also play a role. Anorexic patients, after weight restoration, have required excessive caloric intake to maintain their weight (4, 5). Thus, rapid weight loss in anorexic patients after discharge from the hospital could be due to increased metabolic needs as well as refusal of food. Conversely, bulimic patients studied at a normal body weight have been found to have decreased caloric needs to maintain weight (5, 6). In these patients, a synergism between hyperphagia and hypometabolism (which could promote quick weight gain) may contribute to resumption of binge eating and purging in order to satisfy appetite but avoid weight gain.

There is no consensus about the best method of correcting the caloric requirements of patients with eating disorders for height, weight, and body composition. Clinically, caloric requirements may be expressed as total calories (kcal/day) and total calories corrected for body weight (kcal/kg/day), body surface area (kcal/body surface area/day), body mass index (kcal/body mass index/day), and fat-free mass (kcal/fat-free mass/day).

This study was conducted to confirm and extend previous findings of abnormal caloric utilization in a new and larger group of subjects. In addition, we wanted to explore three disputed issues: 1) whether restricting and bulimic anorexic patients require different caloric intakes to maintain weight after weight restoration (4, 5), 2) whether normal-weight bulimic patients require the same number of calories to maintain stable weight as do previously anorexic bulimic patients (5, 6), and 3) the best method of correcting for body height and weight when determining caloric needs of patients with eating disorders.

METHOD

The subjects were female patients who met the *DSM-III-R* criteria for anorexia nervosa and/or bulimia nervosa and gave written informed consent before participating in the study. All caloric measurements took place while patients were undergoing nutritional monitoring on an inpatient eating disorder unit as part of their treatment. All subjects had been free of medication for

at least 3 weeks prior to the study. It is important to emphasize that all patients were studied when their body weight was within the normal range.

We separated these eating disorder patients into four groups according to their subtype of eating behavior and the length of time they had been at a normal and stable weight. Two groups of anorexic patients, 13 who had anorexia nervosa (anorexia, short-term weight stable) and nine who had both anorexia and bulimia nervosa (anorexia-bulimia, short-term weight stable), had been admitted to the hospital while underweight. The total mean \pm SD length of hospitalization was 111 \pm 31 days for the restricting anorexic patients and 72 \pm 19 days for the bulimic anorexic patients. Daily caloric intake was measured 4 weeks after the patients had reached their target weight (95% of average body weight as determined by the 1959 Metropolitan Life Tables) (22), approximately 2 weeks prior to discharge from our inpatient weight restoration program. Two groups of patients with bulimia, 11 who had previous histories of anorexia nervosa (anorexia-bulimia, long-term weight stable) and 20 who had never had anorexia nervosa (bulimia, long-term weight stable), had been admitted to the hospital while their weight was in a normal range (between 85% and 115% of average body weight). They were studied 1–4 weeks after admission. Bulimic patients with histories of anorexia were hospitalized 50 \pm 24 days, and normal-weight bulimic patients, 46 \pm 17 days. We defined "long-term weight stable" as no anorexic episode (weight <85% of average body weight) within the last 6 months.

All food was supplied by the clinic's metabolic research kitchen. Each food item was weighed before and after meals to determine the number of calories consumed. Anorexic subjects ate three meals, at 8:00 a.m., noon, and 5:00 p.m., and two snacks, at 3:00 and 9:00 p.m. Bulimic subjects ate three meals, at 8:00 a.m., noon, and 5:00 p.m., and one snack at 9:00 p.m. Patients were required to eat all meals within 45 minutes and snacks within 30 minutes; they could not have food at other times or store food in their rooms. Subjects were observed for 1 hour after meals and in the bathroom at all times to prevent vomiting.

Maintenance calories were started at 25 kcal/kg/day for long-term weight-stable patients and 50 kcal/kg/day for short-term weight-stable patients. Over the study period, caloric intake was monitored by a registered dietitian, and meals were adjusted so that patients would maintain a stable weight (± 1.0 kg). Short-term weight-stable patients were required to eat sufficient food to maintain their weight at 95% of average body weight. Long-term weight-stable subjects were not studied during the first 6 days of treatment so that abnormalities of fluid status and inconsistent eating behavior, which are frequently seen during the first days of hospitalization, would not influence study results. Long-term weight-stable patients were required to maintain the weight that had become stabilized after fluid balance had been restored.

Maintenance calories were determined by averaging

TABLE 1. Demographic and Body Composition Characteristics of 53 Patients With Eating Disorders

Variable	Group A: Anorexia, Short-Term Weight Stable (N=13)		Group B: Anorexia- Bulimia, Short-Term Weight Stable (N=9)		Group C: Anorexia- Bulimia, Long-Term Weight Stable (N=11)		Group D: Bulimia, Long-Term Weight Stable (N=20)		F	df	p	Significant ($p < 0.05$) Group Differences
	Mean	SD	Mean	SD	Mean	SD	Mean	SD				
Age (years)	17.3	4.6	22.1	5.2	23.3	5.3	20.7	4.1	3.73	3, 49	0.02	A<C
Duration of illness (years)	2.1	2.4	8.5	4.6	6.9	4.2	5.9	3.4	6.62	3, 49	0.0008	A<B, C, D
Weight (kg)	49.3	4.5	53.7	3.9	54.3	3.4	56.5	4.6	7.63	3, 49	0.0003	A<B, C, D
Height (cm)	158.3	8.3	166.1	5.6	165.8	5.7	163.2	6.1	3.59	3, 49	0.02	A<B, C
Percent of average body weight	94.2	1.8	93.6	2.9	95.1	4.4	101.8	7.3	8.82	3, 49	0.0001	A, B, C<D
Low percent of av- erage body weight	66.5	7.5	76.4	5.0	77.1	5.7	93.6	5.6	56.88	3, 49	0.0000	A<B, C<D
High percent of av- erage body weight	97.1	13.3	117.4	17.9	112.4	19.9	117.6	17.1	4.30	3, 48	0.009	A<D
Current percent of highest weight	98.6	12.1	81.4	13.5	86.4	11.2	87.8	10.8	4.30	3, 47	0.009	A>B
Body mass index	19.7	0.7	19.4	0.6	19.7	0.9	21.2	1.8	6.66	3, 49	0.0007	A, B, C<D
Body surface area	1.5	0.1	1.6	0.1	1.6	0.1	1.6	0.1	5.55	3, 49	0.002	A<B, C, D
Fat-free mass	38.9 ^a	4.8	42.4 ^b	3.0	43.1 ^c	3.3	44.5 ^d	3.2	5.02	3, 36	0.005	A<D

^aN=11.^bN=5.^cN=10.^dN=14.

the calories the patients consumed per day over at least a 7-day weight-stable period. Patients were weighed daily on the same scale. Methods for determining a stable weight have been reported elsewhere (4-6); they involve performing a regression analysis with days as the independent variable and weight as the dependent variable (23, 24). Subjects were considered to have a stable weight if the correlation coefficient was not significant at the $p=0.05$ level for the given time period. Weight data reported in this article represent the mean daily weight for all days of the study period.

Because different methods of correcting for height and weight have been reported (4-6), we corrected caloric intake for weight (kg), for body surface area (body surface area = $0.007184 \times [\text{height (cm)}]^{0.725} \times [\text{weight (kg)}]^{0.425}$) (25), for height and weight, using body mass index (body mass index = $\text{weight [kg]} / \text{height [m]}^2$) (26), and for fat-free mass as determined by skin fold measurements (27, 28).

In the data analysis, tests for normality and equality of variances were performed before parametric analysis. Variables not meeting these criteria were transformed before parametric analysis. Frequencies of binge eating and vomiting were compared by using nonparametric methods. Linear and hierarchical regression analyses were used to assess the relation between patient variables and caloric needs. Multivariate analysis of variance (MANOVA) was used to compare multiple variables between groups. Univariate analysis of variance (ANOVA) and analysis of covariance were conducted, with post hoc two-tailed t tests with the Bonferroni correction for multiple group comparisons. For all significant (by t test) group differences in caloric requirements there was a power of ≥ 0.80 . All statistical

analyses were done using BMDP statistical software (BMDP Statistical Software, Inc., Los Angeles, 1988). Units are expressed as mean \pm SD.

RESULTS

Demographic and Body Composition Characteristics

The demographic and body composition characteristics of the four groups of eating disorder subjects ($N=53$) were compared by ANOVA (table 1). The anorexia, short-term weight-stable group was younger, had a shorter duration of illness, weighed less, and had a lower body surface area than all other groups. They were also shorter in stature than the anorexia-bulimia, short-term weight-stable and long-term weight-stable groups. The bulimia, long-term weight-stable group had a higher percentage of body fat than any other group when this was measured as body mass index; however, the only two groups that differed significantly in terms of fat-free mass were the anorexia, short-term weight-stable and the bulimia, long-term weight-stable groups. The anorexia, short-term weight-stable group had a previous low weight that was lower than that of all other groups, and the bulimia, long-term weight-stable group had a greater previous low weight than that of all other groups. The anorexia, short-term weight-stable group had a lower previous high weight and a higher current weight as a percentage of previous high weight than the bulimia, long-term weight-stable group.

The anorexia, short-term weight-stable group did not have histories of binge eating or vomiting. Weekly

TABLE 2. Caloric Requirements of 53 Patients With Eating Disorders for Stable Weight (± 1.0 kg) Maintenance Corrected for Body Weight, Body Mass Index, Body Surface Area, and Fat-Free Mass

Variable	Group A: Anorexia, Short-Term Weight Stable (N=13)		Group B: Anorexia- Bulimia, Short-Term Weight Stable (N=9)		Group C: Anorexia- Bulimia, Long-Term Weight Stable (N=11)		Group D: Bulimia, Long-Term Weight Stable (N=20)		F	df	p	Significant ($p < 0.05$) Group Differences
	Mean	SD	Mean	SD	Mean	SD	Mean	SD				
Study days	9.0	1.2	8.0	0.9	10.2	2.4	10.4	2.6	3.38	3, 49	0.03	B<D
kcal/day	2419	250	2392	308	1520	124	1456	163	83.63	3, 49	0.0000	A, B>C, D
kcal/kg/day	49.1	2.9	44.4	3.4	28.0	2.0	25.9	3.0	222.97	3, 49	0.0000	A>B>C>D
kcal/body mass index/day	123.4	14.6	122.8	14.0	77.2	8.2	69.1	10.1	83.04	3, 49	0.0000	A, B>C, D
kcal/body sur- face area/day	1633.0	96.7	1501.1	139.0	952.9	59.7	909.9	92.9	196.28	3, 49	0.0000	A>B>C, D
kcal/fat-free mass/day	62.3 ^a	5.2	56.4 ^b	3.9	35.0 ^c	2.7	34.0 ^d	3.3	160.20	3, 36	0.0000	A>B>C, D

^aN=11.^bN=5.^cN=10.^dN=14.

mean \pm SD binge frequencies for the other groups were as follows: anorexia-bulimia, short-term weight stable, 19.3 ± 18.4 (range=0–42); anorexia-bulimia, long-term weight stable, 16.4 ± 11.1 (range=5–35); bulimia, long-term weight stable, 13.3 ± 8.5 (range=3–30). One anorexia-bulimia, short-term weight-stable subject denied binge eating. However, her parents reported that she indulged in multiple binges per week, so she was classified as bulimic, but her binge frequency was listed as zero. Weekly vomiting frequencies were as follows: anorexia-bulimia, short-term weight stable, 19.0 ± 18.8 (range=0–42); anorexia-bulimia, long-term weight stable, 16.1 ± 11.1 (range=5–35); bulimia, long-term weight stable, 12.3 ± 9.2 (range=3–30). There was no difference in terms of binge or vomiting frequency between these three groups.

There was a significant difference in the frequency of amenorrhea or oligomenorrhea between groups (Fisher's exact test, $p=0.001$). At the time of the study, all of the anorexia, short-term weight-stable group were amenorrheic. Seven of nine subjects in the anorexia-bulimia, short-term weight-stable group, nine of 11 in the anorexia-bulimia, long-term weight-stable group, and eight of 20 in the bulimia, long-term weight-stable group had amenorrhea or oligomenorrhea.

A MANOVA was conducted to compare all four groups on age, height, weight, previous low weight as a percentage of average body weight, previous high weight as a percentage of average body weight, current weight as a percentage of previous high weight, duration of illness, number of calories consumed per day, body surface area, and body mass index. The results of this analysis were significant (Wilks's lambda=0.01; $F=15.39$, $df=27$, 120.33 , $p<0.0001$).

Comparisons of Subgroups

Anorexia, short-term weight stable versus anorexia-bulimia, short-term weight stable. For the patients studied

within 4 weeks after the completion of in-hospital weight restoration, the calories necessary to maintain a stable body weight were significantly different for the restricting anorexic patients and the bulimic anorexic patients in terms of kcal/kg/day ($t=3.74$, $df=49$, $p<0.01$), kcal/fat-free mass/day ($t=3.29$, $df=36$, $p<0.01$), and kcal/body surface area/day ($t=2.79$, $df=49$, $p<0.05$) (table 2 and figure 1). In contrast, there was no difference between these groups in terms of kcal/body mass index/day. Using age and low weight as a percentage of average body weight as covariates did not affect group differences, except that when age was used as a covariate in the comparisons of kcal/body surface area/day, the significance of the difference was reduced to a trend.

Anorexia-bulimia, long-term weight stable versus bulimia, long-term weight stable. The two groups of long-term weight-stable patients were of similar weight (table 1) and consumed similar amounts of calories per day. These groups were similar when their daily caloric requirements were corrected for body mass index, body surface area, and fat-free mass (table 2 and figure 1). However, bulimic patients with histories of anorexia nervosa consumed more calories corrected for body weight (kcal/kg/day, table 2) than did those without histories of anorexia nervosa ($t=3.10$, $df=48$, $p<0.05$). This difference continued to be significant when age was used as a covariate, but it was not significant when low weight as a percentage of average body weight was used as a covariate.

Anorexia-bulimia, short-term weight stable versus anorexia-bulimia, long-term weight stable. We studied two groups of bulimic patients with coexisting histories of anorexia nervosa. These two groups were studied at a similar weight. Those studied after short-term weight recovery (within 4 weeks) required significantly more calories (in terms of absolute daily caloric intake or calories adjusted for any correction factor, table 2) to maintain their weight than did those who were long-term (i.e., 3.8 ± 2.5 years; range=0.9–8.8 years) weight

stable. These two groups were similar in age, duration of illness, and previous low and high body weights (table 1). For the long-term weight-stable bulimic anorexic patients, there was no relation between current caloric requirements and the time since their last underweight episode. These findings continued to be significant when age and low weight as a percentage of average body weight were used as covariates.

Relation Between Body Height and Weight and Demographic Variables and Caloric Needs

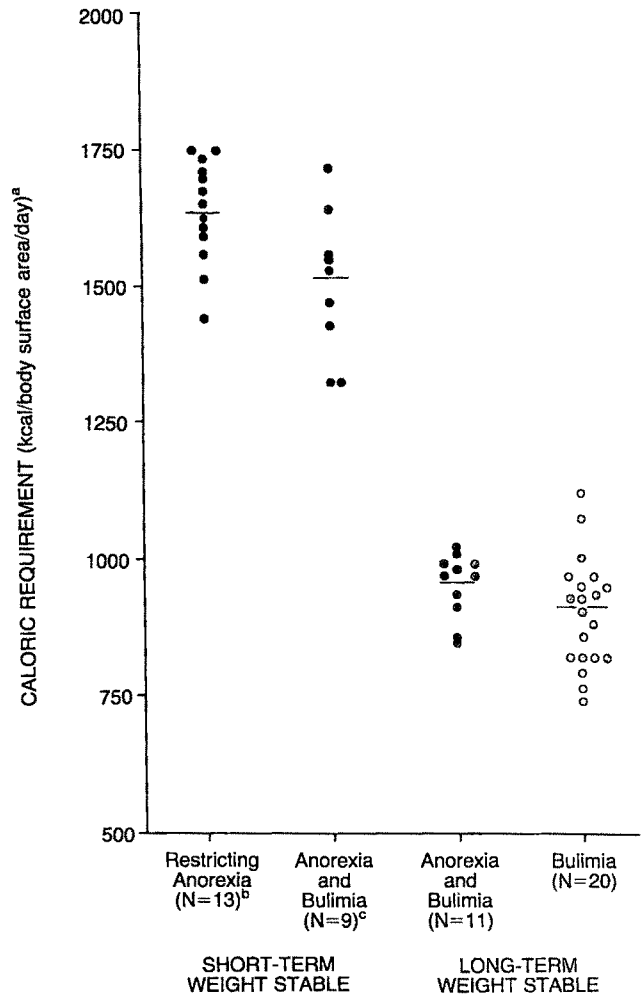
Total caloric intake per day was correlated with body weight, body surface area, body mass index, and fat-free mass (table 3). An analysis was performed with subjects divided into two groups on the basis of whether they were short- or long-term weight stable, and a second analysis was performed with the patients divided into the four groups used to compare caloric requirements. All correlations between body surface area and caloric intake showed significance or a trend toward significance. Weight and fat-free mass were less precisely correlated with caloric intake, whereas body mass index showed no relation to caloric intake. Scatterplots of caloric intake and body correction factors were consistent with a linear relation between caloric intake and body weight correction factors. However, future studies with larger sample sizes are needed to confirm this finding.

For the anorexia-bulimia, short-term weight-stable group, age and duration of illness were significantly ($N=9$, $p \leq 0.05$) correlated with kcal/body surface area/day (age, $r=-0.67$; duration of illness, $r=-0.67$) and kcal/kg/day (age, $r=-0.69$; duration of illness, $r=-0.73$). For the bulimia, long-term weight-stable group, age was correlated with kcal/body mass index/day ($r=-0.45$, $N=20$, $p < 0.05$).

DISCUSSION

This study confirms and extends previous findings of abnormalities in caloric intake among patients with eating disorders. First, we found that in the weeks after weight restoration, restricting anorexic patients had greater caloric requirements than bulimic anorexic patients for all methods of correction of caloric intake except body mass index. Second, when two groups of bulimic patients, those with and those without histories of anorexia nervosa, were studied after being at a stable and normal weight for an extended period of time, a significant difference in caloric requirements between the groups was observed only when the data were expressed as kcal/kg/day. Third, recent weight gain appeared to have a substantial influence on the calories necessary for patients with bulimia and anorexia nervosa to maintain weight. That is, bulimic anorexic patients who were studied within 4 weeks of weight recovery appeared to need about 150% more calories (800 kcal/day) than did an otherwise similar group of bulimic patients with histories of anorexia whose weight

FIGURE 1. Caloric Requirements Corrected for Body Surface Area of 53 Patients in Four Subgroups of Eating Disorders



^aBody surface area = $0.007184 \times [\text{height (cm)}]^{0.725} \times [\text{weight (kg)}]^{0.425}$.

^bAnorexia, short-term weight stable greater than anorexia-bulimia, short-term weight stable ($p < 0.05$) and greater than anorexia-bulimia, long-term weight stable and bulimia, long-term weight stable ($p < 0.01$).

^cAnorexia-bulimia, short-term weight stable greater than anorexia-bulimia, long-term weight stable and bulimia, long-term weight stable ($p < 0.01$).

had been restored for a mean of 3.8 ± 2.5 years. Finally, this study suggests that body surface area may be the best correction factor for caloric intake.

Differences in Caloric Requirements Between Subgroups of Anorexic Patients

Previous studies of short-term weight-restored anorexic patients have conflicting findings. Kaye et al. (4) reported that restricting anorexic subjects needed more calories than bulimic anorexic subjects in terms of kcal/kg/day, kcal/body mass index/day, and kcal/body surface area/day. However, Newman et al. (5) found these groups to be similar in terms of kcal/body mass

TABLE 3. Relation Between Calories per Day Required by 53 Patients With Eating Disorders for Weight Maintenance and Height and Weight Correction Factors

Group	Weight			Body Surface Area			Body Mass Index			Fat-Free Mass		
	N	r	p	N	r	p	N	r	p	N	r	p
Anorexia and anorexia-bulimia, short-term weight stable	22	0.70	<0.01	22	0.67	<0.01	22	0.06	0.79	16	0.65	<0.01
Anorexia-bulimia and bulimia, long-term weight stable	31	0.31	0.09	31	0.44	0.01	31	-0.12	0.53	24	0.40	0.05
Anorexia, short-term weight stable	13	0.82	<0.01	13	0.83	<0.01	13	-0.32	0.29	11	0.75	<0.01
Anorexia-bulimia, short-term weight stable	9	0.84	<0.01	9	0.78	0.01	9	0.60	0.09	5	0.63	0.25
Anorexia-bulimia, long-term weight stable	11	0.49	0.12	11	0.62	0.04	11	-0.29	0.38	10	0.47	0.17
Bulimia, long-term weight stable	20	0.34	0.14	20	0.41	0.08	20	0.01	0.95	14	0.37	0.19

index/day. We found that restricting anorexic patients had significantly greater caloric needs than bulimic anorexic patients when caloric intake was corrected for body weight, body surface area, and fat-free mass. However, we found no difference between groups when caloric intake was corrected for body mass index. It is possible that discrepancies among the findings of different groups of investigators are related to the methods used to correct for daily caloric intake.

In this study the restricting anorexic patients were younger than the bulimic anorexic patients. Since caloric requirements decrease with age (29), it is possible that the differences between these two groups were related to differences in age. Age was not significantly correlated with caloric requirements within any of the four subgroups; however, when age was used as a covariate in the analysis of caloric requirements, the significance of the difference between restricting and bulimic anorexic patients was less substantial. Future studies using either larger sample sizes or restricting and bulimic anorexic subjects matched for age would be necessary to investigate this finding.

We did not study healthy volunteer women. Nevertheless, the magnitude of the caloric intake necessary for weight maintenance in patients with anorexia nervosa, whatever the correction factor, was well in excess of caloric requirements for healthy control women (4).

Differences in Caloric Requirements Between Subgroups of Bulimic Patients

Gwirtsman et al. (6), using kcal/kg/day and kg/body mass index/day, found that long-term weight-stable anorexic bulimic patients were similar in caloric requirements to bulimic patients with no previous history of anorexia. In contrast, Newman et al. (5), using kcal/body mass index/day, found that previously anorexic bulimic patients needed significantly more calories than nonanorexic bulimic patients. We found that the possibility of differences between these bulimic subgroups, matched for age and weight, depended on the methods used to correct daily caloric intake. Previously anorexic bulimic patients needed more calories than nonanorexic bulimic patients when kcal/kg/day was used, but these groups were similar in terms of total kcal/day and total kcal/day corrected for body surface area, body mass index, and fat-free mass.

Newman et al. (5) found that the daily caloric intake of bulimic patients was positively related to age and negatively related to previous high body weight. In contrast, we found no relation between age and caloric needs and, like Gwirtsman et al. (6), we did not find that previous high weight influenced caloric requirements.

Gwirtsman et al. (6) compared their patients to matched healthy control volunteers studied under similar conditions. They found that both anorexic bulimic and bulimic patients needed significantly fewer calories than volunteers to maintain a stable weight. We were not able to study healthy volunteer women and thus cannot determine whether caloric intake for the bulimic women in this study was less than for healthy matched control subjects.

Relation of Recent Weight Gain to Caloric Needs in Anorexic Bulimic Patients

An important question raised by this study is whether abnormalities of caloric intake represent a state-related (presence or absence of recent weight gain) or a trait-related phenomenon. We compared two groups of anorexic bulimic patients who were at similar weight and lean body mass. The short-term weight-stable group (who were studied within 4 weeks after weight restoration) needed a significantly greater daily caloric intake than did the long-term weight-stable group (studied an average of 3.8 ± 2.5 years after recovery from an anorexic episode). These findings agree with previous reports (4, 5) suggesting that inflated caloric needs in the short-term period are likely to be state related.

Most Useful Body Size Correction Factor for Determining Caloric Needs

It is not certain which method of correcting for different body heights and weights among patients is most useful for patients with eating disorders (4-6). If it is assumed that the subgroups of eating disorder patients are similar in terms of their metabolic needs, then energy utilization (daily caloric intake) should be proportional to body mass. Our data suggest that, when controlling for the presence or absence of recent weight gain, body surface area may be the best correction factor for determining the caloric needs of eating disorder patients. We found that absolute body weight and fat-

free mass were correlated relatively less well with caloric needs and that body mass index was poorly correlated with caloric needs.

The finding that body surface area was positively related to caloric intake makes sense, since body surface area is a physiologically derived factor that has been shown to be related to resting metabolic rate and lean body mass (30). Body mass index appears to be a less precise approximation of the relative relation of height and weight to caloric needs (31).

Several points about our data should be noted. First, physical activity, which has been shown to contribute to energy needs in patients with eating disorders (32) and other subjects (33), may alter the relation between caloric intake and body mass. Second, we began feeding patients a prescribed amount of kcal/kg/day and then adjusted caloric intake depending on changes in daily body weight. While kcal/kg/day was not the most precise correction factor, it is possible that our method of prescribing caloric intake biased relationships to other correction factors. Finally, it is possible that skin fold measurements may be somewhat inaccurate in measuring fat-free mass and thus invalidate the use of this correction factor.

Significance of Altered Caloric Needs in Patients With Eating Disorders

These findings are of clinical importance in the treatment of patients with anorexia nervosa. These patients have a high relapse rate (1). Presumably, a high rate of relapse occurs because anorexic patients frequently remain resistant to consuming sufficient calories after recovery. Our findings suggest that another factor, abnormally high caloric requirements for weight maintenance, also plays a significant role in rapid weight loss and relapse after discharge from inpatient treatment. Restricting and bulimic anorexic patients require 45–50 kcal/kg/day, compared to approximately 30 kcal/kg/day reported for healthy control subjects (6). Thus, before discharge, patients with anorexia nervosa should learn about and practice consuming the large amount of calories they appear to need to maintain their weight in the short term. Such treatment has the potential of reducing the high rate of relapse in this illness.

This study could not determine whether normal-weight bulimic patients have lower caloric needs, because we did not have a normal comparison group. However, studies of caloric utilization (6) and of metabolic rate (34, 35) suggest that normal-weight bulimic women may have reduced energy needs. The difference in caloric requirements for weight maintenance between normal-weight bulimic women and healthy volunteers is less extreme than that seen in anorexic patients. For a normal-weight bulimic woman without a history of anorexia who weighs 50 kg, the difference in caloric needs may translate into several hundred calories per day less than for a peer without an eating disorder. It remains uncertain whether normal-weight bulimic women are not adequately satiated when consuming

reduced calories (which may be necessary to maintain a stable weight), but this may contribute to an increased urge to binge eat. Conversely, prescribing a normal caloric intake may cause weight gain and contribute to bulimic patients' resuming purging as a means of weight control.

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Absence of Linkage Between Chromosome 11p15 Markers and Manic-Depressive Illness in a Belgian Pedigree

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Objective: The original finding of genetic linkage in an Old Order Amish pedigree has been contradicted by the results of several subsequent studies. Using the same genetic parameter values, diagnostic criteria, and 11p15 genetic markers as those used to study the initial Amish population, the authors performed a linkage study of a four-generation informative pedigree in Belgium. **Method:** Recombinant DNA technology was used to analyze three markers for the chromosome 11p15 location: the genes for tyrosine hydroxylase (TH) and insulin (INS), and the c-Harvey-ras oncogene (HRAS). Diagnoses of the relatives of a proband with bipolar affective disorder were determined with the Schedule for Affective Disorders and Schizophrenia—Lifetime Version and based on the Research Diagnostic Criteria. Relatives were considered affected if they had bipolar disorder, unipolar disorder, or cyclothymia; a diagnostic hierarchy was developed to include unipolar disorder and cyclothymia in the linkage analysis. **Results:** Pairwise analyses of the disease locus and each of the three polymorphisms excluded the possibility of close linkage between manic-depressive illness and the three chromosome 11p15 markers. Multipoint linkage analysis combining the information from all three genes also excluded linkage. **Conclusions:** The conflict between the original results from the Amish study and the many negative reports on chromosome 11 linkage of manic-depression has been interpreted as indicating genetic heterogeneity, but heterogeneity has not been documented for the 11p15 locus. Conversely, the linkage approach has major drawbacks, so other genetic strategies should also be considered.

(Am J Psychiatry 1991; 148:1683–1687)

Manic-depressive illness, characterized by major depressive episodes alternating with phases of mania or hypomania, is a severe and common disease, affecting 1% of the general population. Family, twin, and adoption studies have suggested the involvement of genetic factors in the etiology of affective disorders (1).

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Supported by grants from the National Fund for Scientific Research and the Flemish Biotechnology Program, Belgium, and the National Center for Scientific Research, the National Institute for Medical Research, and the Ministry of Research and Technology, France.

The authors thank P. Raeymaekers and L. Sandkuijl for help with the linkage analysis and C. Delarbre, J.H. Van Houche, and D. Durand for technical help and data collection.

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The identification of genes for susceptibility to disease can now be conveniently approached through recombinant DNA technology. To date, claims of genetic linkage in families of bipolar patients have focused on two chromosomal locations: one on the X chromosome and the other on chromosome 11. First, linkage to the gene for coagulation factor IX in the subterminal region of the long arm of the X chromosome (2) has supplemented findings from previous studies using non-DNA markers (3–7). Second, two markers, the c-Harvey-ras oncogene (HRAS) and the insulin gene (INS), have been shown to cosegregate with the disease trait in an Old Order Amish pedigree (8, 9). These two markers are located on the tip of the short arm of chromosome 11 (11p15) and are closely linked to the gene encoding tyrosine hydroxylase (TH) (10), the rate-limiting enzyme for the synthesis of catecholamines. However, X-linkage with either classical markers (11) or DNA polymorphisms (12) has not been consistently reported. The chromosome 11 location was not found in three North American families (13), three Icelandic families (14), an

TABLE 1. Characteristics of Three 11p15 Markers Used in Linkage Analysis of Affective Disorders in a Belgian Family

Gene	Probe	Restriction Enzyme	Allele Lengths (kb)	Allele Frequencies ^a
TH	pJ4.7	Taq I	4.8	0.22
			2.8+2.0	0.78
HRAS	pUC EJ6.6	BamHI	8.0	0.11
			7.5	0.11
			6.9	0.78
INS	phins310	Pvu II	2.3	0.31
			0.83	0.64
			0.76	0.05

^aThe allele frequencies were calculated from the nine married-in individuals in the pedigree.

Irish pedigree (15), or two Australian pedigrees (16). In addition, a recent reanalysis of this Old Order Amish pedigree (17), which included a large lateral extension of the original pedigree and two changes in clinical status, excluded linkage between bipolar illness and the *HRAS* and *INS* genes. These apparent discrepancies can be interpreted in at least two ways: there is genetic heterogeneity, even among the Old Order Amish, increasing the complexity of genetic analysis, and/or there is strong evidence against the existence of a locus for susceptibility to manic-depressive illness in the region of 11p15. However, it should be emphasized that the statistical significance of the initial positive linkage found in the Old Order Amish pedigree remains difficult to interpret because multiple tests have been performed with different genetic models, different classification criteria, and various sets of markers distributed throughout the genome (18, 19). This "multiple testing," nowadays classically used in linkage studies of complex diseases with unknown modes of inheritance and unclear phenotype definitions, could enhance the probability of finding a lod score exceeding 3 in the absence of linkage between disease and marker (20). Therefore, proof of the existence of a locus for predisposition to manic-depressive illness in the 11p15 region requires a new analysis of a different pedigree, using the same genetic parameter values, the same diagnostic criteria, and the same 11p15 genetic markers as those used for the initial Amish population (9, 17).

METHOD

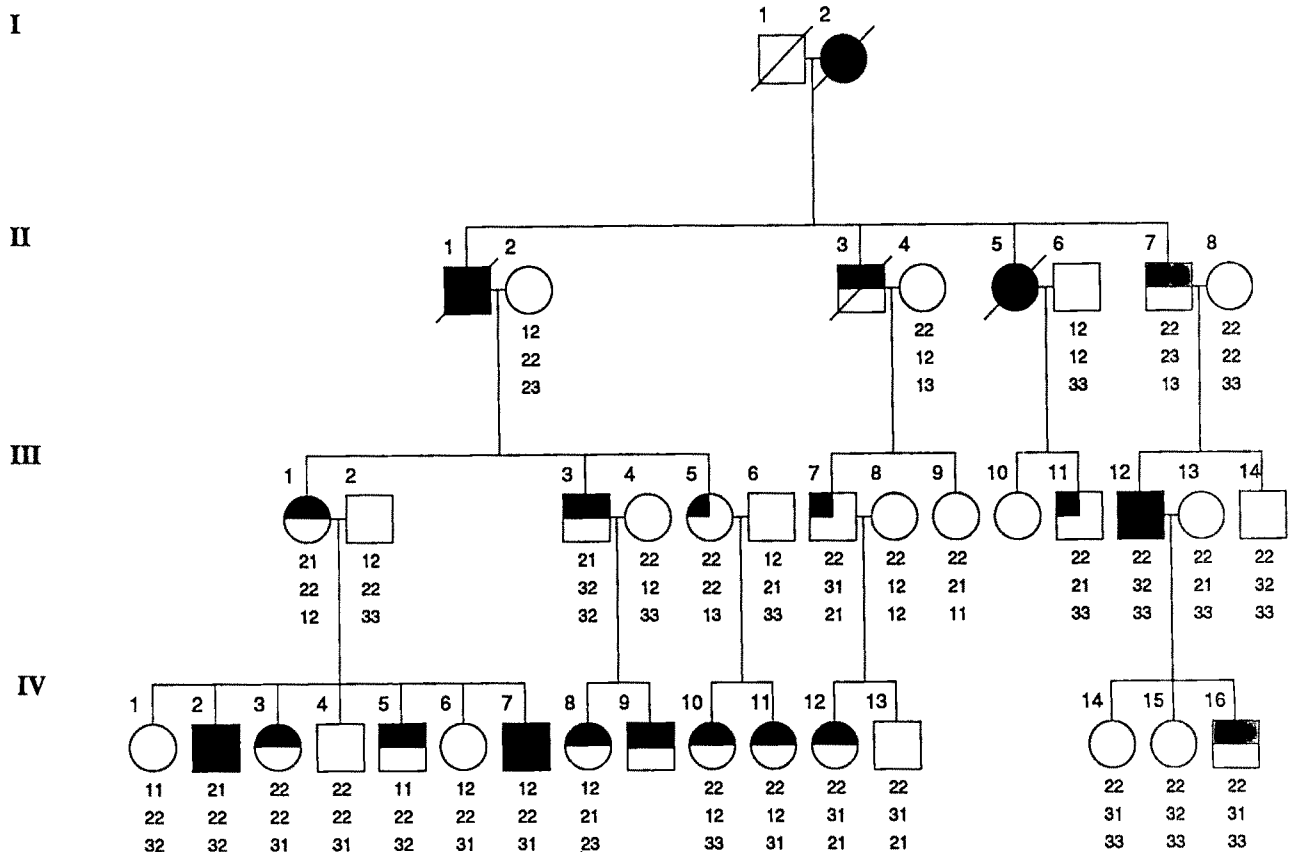
We identified a large, multigeneration, multiply affected Jewish Ashkenazi family originating in Poland. After giving informed consent, the proband and all available relatives were personally examined by two interviewers (S.S., D.H.) using a semistructured interview, the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (21), which provides diagnoses based on the Research Diagnostic Criteria (RDC) (22). Information from relatives and medical and social records was also used when available. A good interrater reliability was found between

the interviewers during a World Health Organization international multicenter study (23). Assessment of the family members was performed by investigators who were blind to the proband's diagnosis. Disagreements about the relatives' diagnoses were referred to the senior investigator (J. Mendlewicz), who determined the final diagnoses blindly. Any subject with a diagnosis of bipolar disorder, unipolar disorder, or cyclothymia (i.e., primary affective disorder) (24) was considered affected. The inclusion of cyclothymia in the affective disorder spectrum for the purpose of linkage analysis is justified by findings that cyclothymia is significantly more prevalent in the relatives of bipolar patients than in the relatives of comparison subjects (25, 26). Further, the prevalence of bipolar illness in first-degree relatives of cyclothymic patients is similar to the prevalence observed in the relatives of bipolar patients (27). Subjects with secondary depression, minor depression, alcoholism, or drug dependence were considered unaffected.

To avoid possible interference of diagnosis with linkage results, the DNA marker analysis was performed by investigators who were blind to the results of the psychopathological evaluation. In addition, Southern blots were performed in duplicate in two different laboratories (A.D.B. in Belgium and A.M. in France). Genomic DNA extracted from leukocytes was digested with *Bam*HI, *Taq* I, and *Pvu* II restriction enzymes, separated by electrophoresis on a 0.8% agarose gel (28) and transferred to nylon filters by Southern blotting (29). At the *TH* locus, a 4.7-kb genomic fragment (pJ4.7) was used to detect a *Taq* I dimorphism (30). A 9.0-kb *INS* genomic fragment (phins310) identified the *Pvu* II polymorphism (31). Finally, at the *HRAS* locus a pUC EJ6.6 probe was used to detect a *Bam*HI triallelic polymorphism (32). The phins310 and pEJ6.6 probes were obtained from the American Type Culture Collection. Descriptions of the genetic markers are given in table 1. The *TH*, *INS*, and *HRAS* alleles in the pedigree are displayed in figure 1, together with the diagnoses of all available relatives.

The paternity of all members in the family was confirmed by Southern blot hybridization of *Hinf*I-digested DNA with the multiallelic minisatellite probe 33.15 (33) and with three diallelic minisatellite probes—MS8, MS31, and MS43 (34).

To determine the significance of cosegregation of the *TH*, *INS*, and *HRAS* genes with a gene for susceptibility to bipolar affective disorder, linkage analysis was performed with the linkage programs MLINK and LINKMAP of the LINKAGE package, version 5.03 (35). The same genetic parameter values as those inferred from the segregation analysis of the Amish population (9, 17) were used in the analysis. This model assumes an autosomal mode of inheritance with a disease allele frequency of 0.015 and age-specific penetrance defined by four liability classes (15–19 years, 0.18; 20–24 years, 0.42; 25–29 years, 0.73; 30 or more years, 0.85). The normal genotype was estimated to have a penetrance of 0.0001 for liability

FIGURE 1. Pedigree of Belgian Proband With Bipolar Affective Disorder^a

^aSquare=male, circle=female; filled symbol=bipolar, half-filled=unipolar, quarter-filled=cyclothymic, open=unaffected. The alleles are indicated by the numbers below the symbols and correspond to the allele lengths in table 1. The order of the probes from top to bottom is TH, INS, and HRAS.

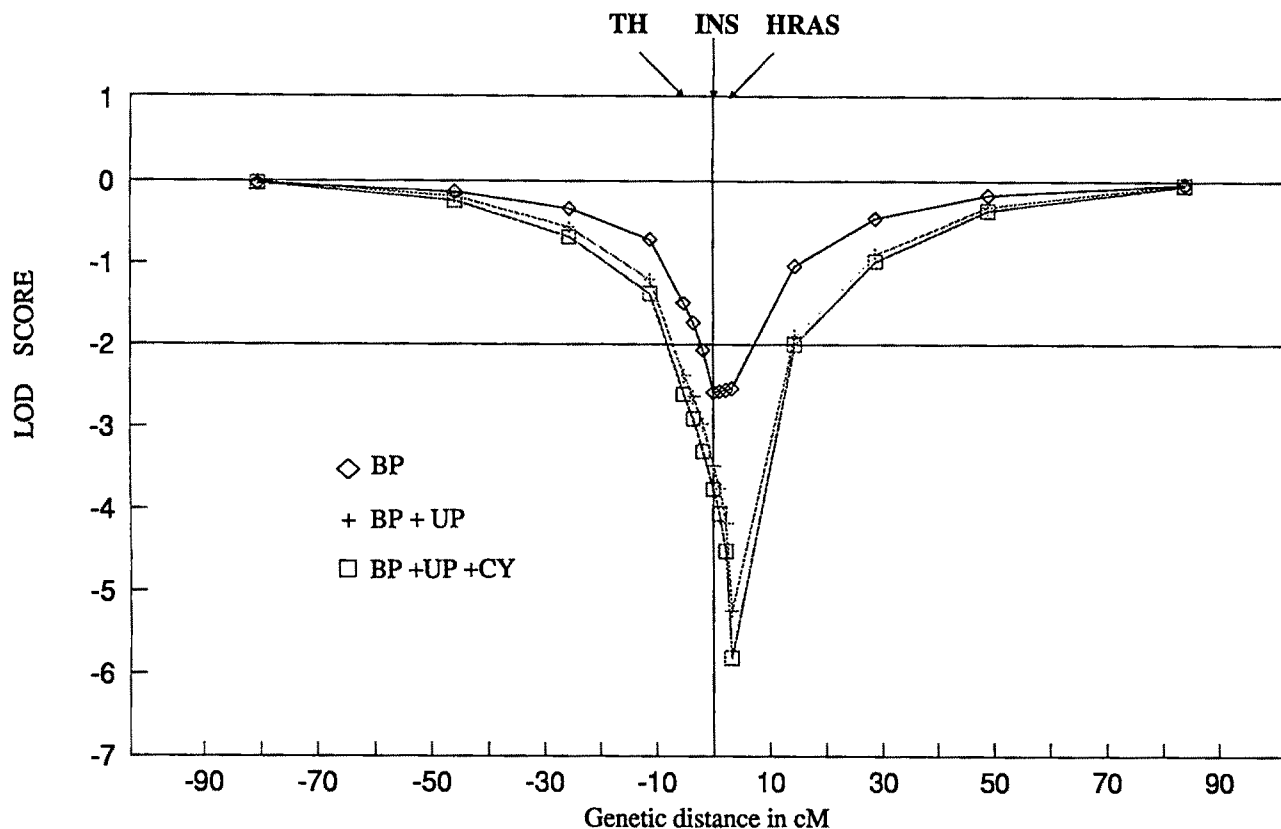
TABLE 2. Two-Point Lod Scores for Belgian Family Based on Different Clinical Thresholds for Affective Disorder

Locus and Diagnoses Included	Lod Score for Each Recombination Fraction (θ)						
	$\theta=0.00$	$\theta=0.01$	$\theta=0.05$	$\theta=0.1$	$\theta=0.2$	$\theta=0.3$	$\theta=0.4$
TH							
Bipolar	0.07	0.07	0.06	0.06	0.04	0.03	0.01
Bipolar, unipolar	-1.01	-1.00	-0.9	-0.72	-0.41	-0.21	-0.08
Bipolar, unipolar, cyclothymic	-1.00	-0.99	-0.89	-0.71	-0.41	-0.21	-0.08
INS							
Bipolar	-1.82	-1.31	-0.75	-0.48	-0.23	-0.10	-0.03
Bipolar, unipolar	-1.16	-1.09	-0.85	-0.58	-0.21	-0.02	0.04
Bipolar, unipolar, cyclothymic	-1.71	-1.58	-1.19	-0.84	-0.33	-0.07	0.03
HRAS							
Bipolar	-2.30	-2.16	-1.43	-0.90	-0.37	-0.13	-0.02
Bipolar, unipolar	-5.37	-4.34	-2.95	-2.08	-0.99	-0.38	-0.08
Bipolar, unipolar, cyclothymic	-5.36	-4.68	-3.23	-2.21	-1.02	-0.38	-0.08

class 1 and of 0.001 for all others. Two healthy relatives younger than 14 years were considered to have unknown phenotypes. Because our pedigree includes a number of individuals with unipolar disorder and cyclothymia, which may or may not be genetically related to bipolar disorder, a diagnostic hierarchy was developed to include such individuals in the linkage analysis. This three-dimensional strategy follows the classification used in the Amish study (17).

RESULTS

Pairwise analyses of the disease locus and each of the three polymorphisms excluded the possibility of close linkage between manic-depressive illness and the three chromosome 11p15 markers, given the assumption that an autosomal dominant gene is responsible for the disease susceptibility in the family (table 2). The lod scores were negative for all of the genotypes studied,

FIGURE 2. Multipoint Linkage Analysis of Belgian Family Using Different Clinical Thresholds for Affective Disorder^a

^aBP=bipolar disorder, UP=unipolar disorder, CY=cyclothymia.

with the exception of a positive lod score of 0.07 at a recombination fraction $\theta=0.0$ in bipolar subjects only.

Multipoint linkage analysis combining the information from all three genes (*TH*, *INS*, and *HRAS*) also excluded linkage. Under the assumption of autosomal dominance, the exclusion regions were 8.9 cM, 22.2 cM, and 23.6 cM of chromosome 11p with, respectively, the bipolar, bipolar-unipolar, and bipolar-unipolar-cyclothymic diagnostic models (figure 2). The order of the markers in the multipoint analysis was *cen-TH-INS-HRAS-tel*; the distance between the *TH* and *INS* genes was fixed at $\theta=0.05$, and the distance between the *INS* and *HRAS* genes was fixed at $\theta=0.031$ (36). The exclusion results were not significantly different if *TH* was placed either between *INS* and *HRAS* or distal of *HRAS*. No obligate recombinants were detected between *TH* and *INS*, *TH* and *HRAS*, or *INS* and *HRAS*.

DISCUSSION

The results of our linkage analysis of a large, informative, multigeneration kindred ascertained in Belgium rules out tight linkage between three chromosome 11p15 markers and a gene predisposing to manic-depressive illness. The negative reports on chromosome 11 linkage of manic-depression from North America,

Europe, and Australia (13–16), the present study, and the lack of replication of the original findings from the Amish study (17) call into question the existence of a locus for susceptibility to bipolar disorder in the chromosome 11p15 region. These conflicting results have been interpreted as indicating genetic heterogeneity, which has been documented for the X-linked form of bipolar illness (37, 38) but not for the 11p15 locus. Conversely, although linkage strategies in complex non-Mendelian behavioral diseases are useful, it is difficult to ascertain large, multigeneration, informative families and there are no objective criteria for differentiating affected from nonaffected subjects. Furthermore, neither the number of disease susceptibility genes nor the mode(s) of transmission of major psychiatric disorders has yet been clearly defined. The current enthusiasm for the linkage approach in psychiatry might thus be counterproductive if other genetic strategies, such as the sib pair method and association studies, are not being considered.

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How the Medical Comorbidity of Depressed Patients Differs Across Health Care Settings: Results From the Medical Outcomes Study

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***Objective:** Although depression is one of the most common problems of medical and psychiatric outpatients, it has not been clear whether the extent of medical comorbidity among depressed patients varies across major types of clinical settings in which depressed patients receive care—especially by type of treating clinician (general medical versus mental health specialty) or type of payment for services (prepaid versus fee-for-service). **Method:** The authors examined these issues using data on 1,152 adult outpatients with current depressive symptoms and a lifetime history of unipolar depressive disorder who received care in one of three health care delivery systems in three U.S. sites. **Results:** Depressed patients had a similarly high prevalence (64.9%–71.0%) of any of eight common chronic medical conditions whether they were seen in the general medical or specialty mental health sector; however, those visiting medical clinicians had a significantly higher prevalence of the two most common chronic medical conditions, hypertension and arthritis. Among depressed patients with hypertension, those visiting the general medical sector were more likely to be taking antihypertensive medication than were those visiting the mental health specialty sector. Type of payment (prepaid versus fee-for-service) was unrelated to either prevalence or severity of comorbid medical conditions, suggesting that the typical depressed patient in all types of practices studied had medical comorbidity. **Conclusions:** These data suggest that clinicians in all health care settings must be prepared to encounter chronic medical conditions and complaints in the depressed patients who visit them.*

(Am J Psychiatry 1991; 148:1688–1696)

Over the last 20 years, a large body of research has documented that depression, as defined by level of depressive symptoms or prevalence of specific depressive disorders, is one of the most common health problems of outpatients visiting general medical clinicians and mental health specialists (1–7). Further, a large literature documents a high rate of co-occurrence of depression and chronic medical conditions such as hyper-

tension, diabetes, and heart disease (8–11). Nevertheless, it has been uncertain how the medical comorbidity of depressed patients varies across the different types of settings in which they receive care. For example, it is known that about one-half of individuals with psychiatric disorders in the United States have their only health care contact with the general medical sector (12, 13). Are such patients relatively more medically ill than persons with comparable psychiatric disorders who receive care from mental health specialists? If so, then different approaches to treating depression may be indicated in the two types of practices and different resources for providing treatment would be required.

A similar set of issues applies to depressed patients who receive care in practices that rely on different mechanisms for financing care. The United States now has a pluralistic health care delivery “system,” especially in the private sector. The once predominant solo, fee-for-service style of practice now actively competes with other forms of practice, but especially with prepaid care. Some have suggested that mental health care

Received July 10, 1989; revision received March 19, 1991; accepted June 17, 1991. From the RAND Corporation, the Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, Neuropsychiatric Institute and Hospital and School of Medicine, and the Institute for the Improvement of Medical Care and Health, New England Medical Center Hospitals, Boston. Address reprint requests to Dr. Wells, RAND, 1700 Main St., Santa Monica, CA 90407-2138.

Supported by grants from the Robert Wood Johnson Foundation, the Henry J. Kaiser Family Foundation, the Pew Charitable Trusts, NIMH, and the RAND Corporation out of its own research funds.

The conclusions are those of the authors and do not necessarily reflect the opinion of the sponsors or the authors' institutions.

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may cost less in prepaid plans than in fee-for-service insurance partly because prepaid plans enroll individuals who are less sick (14, 15). If this explanation is true, then one might expect depressed patients who receive care in prepaid practices to be less sick, including having less medical comorbidity, than their counterparts in fee-for-service plans. Alternatively, if prepaid practices lower overall costs through lowering the intensity of services provided patients with minor illnesses, one might expect to observe greater medical comorbidity for the average depressed patient seen in these settings.

Further, the distribution of medical comorbidity among depressed patients across health care settings could reflect effects of interactions between type of provider and type of payment. For example, if prepaid practices reserve the use of mental health specialists for their most complicated depressed patients but rely on general medical providers to screen all patients, then one might expect greater medical comorbidity in prepaid than in fee-for-service settings only among mental health specialty patients.

Any of the above postulated differences in medical comorbidity could have important clinical and policy implications. For example, the settings treating patients with relatively greater medical comorbidity might need to rely more on careful coordination of care between the mental health specialty and general medical sectors (16, 17). Further, some studies suggested that medically ill depressed patients are particularly difficult to evaluate and treat (16–19); thus one might also expect higher costs of care and possibly worse outcomes, on average, for depressed patients with greater medical comorbidity, although one study reported more favorable outcomes for depression secondary to medical conditions than for depression secondary to other psychiatric conditions (20).

Given that the National Institute of Mental Health (NIMH), through its Depression Awareness, Recognition, and Treatment Program (21), is currently engaged in informing both the general public and clinicians about the importance of recognizing and treating depression, it is particularly timely to understand how the clinical characteristics of depressed patients vary across the major health care delivery systems in the United States. In this paper, we address this issue by comparing the prevalence of chronic medical conditions in depressed patients who receive care from mental health specialists or general medical clinicians and whose care is financed by prepaid versus fee-for-service arrangements. To our knowledge, this is the first effort to provide such comparisons.

The context for our paper includes extensive literatures on the association between depression and specific medical illnesses in treated and general population samples (1–11, 22–28), on the treatment implications of depression in seriously medically ill patients (1, 9–11, 16–19, 22–25, 29–31), and on differences in the general health status of patients receiving prepaid or fee-for-service care or visiting different provider sectors (14, 32, 33). It is beyond the scope of this paper to re-

view these literatures in detail. Instead, we comment on findings that are particularly germane to comparisons by type of health care setting.

Clinical studies of the relationship between depression and medical illnesses suggested that patients with many specific serious medical conditions have a high rate of depression and vice versa (8, 9, 34, 35). Studies of general populations confirmed this overall conclusion (8, 26). Further, studies suggested that medical clinicians often fail to detect depression or to institute appropriate treatment, especially when comorbid medical conditions are present (3, 9, 35–38), and that mental health clinicians often fail to detect comorbid medical illnesses in patients with serious psychiatric disorders (39, 40). Numerous studies described the challenges facing clinicians in assessing and treating depression in medically ill patients, and some provided suggestions for such treatment (1, 16–19, 29–31). Some studies on the outcomes of treatment for depression in medically ill patients exist (18, 20, 41), but most investigators have commented on the need for further data on outcomes (9, 42).

Studies of health services that compared the clinical characteristics of patients treated in different health care settings have reached conflicting conclusions. Studies of populations enrolled in prepaid or fee-for-service plans have found few differences in health status, including level of psychological distress (33, 34, 43), prevalence of psychiatric disorder, and level of depressive symptoms (44). Studies of treated populations, however, suggested that psychiatric patients in fee-for-service practices may be relatively sicker than those treated in health maintenance organizations (HMOs) (14). Studies contrasting patients of mental health specialists and general medical providers have tended to focus on level of psychopathology. For example, Coulehan et al. (45) found similar levels of depressive symptoms and Wells et al. (46) found similar levels of psychological distress in patients treated by the different providers, but most studies based on chart reviews or claims forms suggested that mental health specialty patients have more serious psychiatric diagnoses (47, 48).

Because of differences in methods across studies and other study limitations, it has been difficult or impossible to draw conclusions on how medical comorbidity of depressed patients varies across varying types of treatment settings.

In the current study, we examined the data on depressed patients who received ongoing care (not necessarily for depression) in one of three different health care delivery systems in three U.S. sites. We used the same criteria to define and identify depression and medical comorbidity across settings. We relied on a definition of depression based on *DSM-III* and conducted case finding using the NIMH Diagnostic Interview Schedule (DIS) (49). We relied primarily on a patient self-report survey measure to identify chronic medical conditions and complaints, but for some conditions, we compared patient reports with assessments by the treating clinician and by independent study clinicians.

METHOD

The data are from the baseline assessment of patients with depressive disorder who participated in the National Study of Medical Care Outcomes (the Medical Outcomes Study), an observational study of adult patients who receive care in one of three health systems: HMOs, large multispecialty group practices with mixed prepaid and fee-for-service coverage, and small single-specialty group and solo practices with fee-for-service or prepaid (independent practice association) coverage. The baseline assessment occurred at the time of and shortly after an office visit to a clinician practicing in these systems of care in Los Angeles, Boston, and Chicago (50, 51).

At each site, one large HMO and several group practices were selected. The group practices were required to have at least 10 clinicians and at least 10% of their practice income due to prepayment. Solo/single-specialty group providers were identified who practiced in the same geographic regions as the HMOs and multiple-specialty group practices. Within each selected system of care, a representative sample of providers was selected. Among participating providers, a representative cross-section of their patients was screened for depressive disorder.

The Medical Outcomes Study clinician sample included internists, family practitioners, cardiologists, endocrinologists, diabetologists, psychiatrists, and psychologists. Within each specialty, eligible clinicians were between the ages of 31 and 55, Board eligible or Board certified or licensed for independent practice, and had direct patient care as their primary professional activity.

The Medical Outcomes Study attempted to enroll all eligible clinicians in the participating HMOs and group practices. Clinician eligibility was determined by information provided by the group practices, confirmed by telephone interviews of clinicians. The HMOs and group practices included 266 eligible clinicians, of whom 225 (85%) agreed to participate in the Medical Outcomes Study. In the solo/single-specialty group practice sector, clinicians were selected by a multistage sampling process that yielded 674 eligible and selected clinicians (based on design priorities such as clinical specialty and proximity of practice zip code to the zip codes for the group practices) for final screening by study staff. At this phase, 79 could not be contacted and 46 refused further participation. An additional 38 clinicians were eliminated because more clinicians agreed to participate in some practice/specialty groups than were needed for the study. Of the 511 remaining clinicians, 298 (58%) agreed to participate in the main study and actually screened their patients. The total number of participating clinicians in all settings was 523.

We conducted extensive comparisons of participants and nonparticipants in the solo sector (51). We found that participation was unrelated to demographic factors of clinicians, clinical specialty, or level of previous training. Participants tended to be more involved in direct patient care. Questionnaires completed by clinician participants and nonparticipants indicated that the decision to enroll

in the study was unrelated to the clinician's past experiences and attitudes toward depressed patients and treatment of depression. Therefore, we think that clinician nonresponse is unlikely to seriously bias the estimates reported here. Nevertheless, we weighted the data for the probability of clinician response.

Participating clinicians were asked to request that all adult English-speaking patients who visited their practice over a several-day period complete a short self-report questionnaire (the Patient Screener). However, in very-high-volume group practices, every other patient visiting the practice was asked to complete the questionnaire because there were more patients than necessary to represent the practice. The Patient Screener was designed to determine eligibility for a longitudinal phase of the study. (Eligibility requirements for the longitudinal study were that patients have one of the Medical Outcomes Study tracer conditions, have an ongoing relationship with the Medical Outcomes Study clinician, be able to complete self-administered questionnaires, and not have specific acute physical conditions that could temporarily severely limit their functioning.) Complete questionnaires were obtained for 12,571 (75%) of the 16,867 eligible patient visitors to HMO and group practices and from 9,828 (65%) of the 15,054 such visitors to solo practices. The total number of participating patients was 22,399.

Two versions of the Patient Screener were used, each administered to a random 50% of patients. One version, completed by 11,242 patients, elicited information on well-being, functioning, and selected chronic medical conditions.

Diagnoses of Depressive Disorder and Other Patient Characteristics

To facilitate identifying cases of depressive disorder in such a large patient sample, we used a two-stage case finding procedure. In the first stage, patients completed an eight-item self-administered depression symptom screener as part of the Patient Screener. The symptom screener elicits information on intensity of depressive symptoms in the past month and on periods of depressed mood over the past 12 months. It has excellent sensitivity and acceptable positive predictive value for identifying *DSM-III* major depression and/or dysthymia (52). At the second stage, patients who exceeded a cutoff score on the depression symptom screener were contacted for a follow-up telephone interview that included the depression section of the DIS (49). The telephone interview was limited to respondents who met the eligibility requirements for a longitudinal phase of the Medical Outcomes Study. Wells et al. (53) provided evidence that telephone and face-to-face administration of the DIS are equivalent for assessing lifetime depressive disorder.

Among the 22,399 patients in the cross-sectional sample, 4,813 exceeded the cutoff for probable depression on the first-stage screener. Of these 4,813 patients, 3,663 met the Medical Outcomes Study criteria. Of

these 3,663 patients, 2,262 (62%) completed the telephone DIS interview. Nonresponders to the telephone interview were slightly less educated, were more likely to be married and female, were more likely to be from fee-for-service practices, had slightly higher depression scores, and were slightly less likely ever to have had diabetes. However, there were no significant differences by specialty or interactions among specialty, payment, and depression scores. We accounted for nonresponse in our analyses by weighting and by including variables related to nonresponse as covariates.

We used data from the telephone-administered depression section of the DIS to identify patients with depressive disorders. In this paper, we focus on patients who met *DSM-III* criteria for a lifetime diagnosis of major depression or dysthymia. We excluded those with a lifetime diagnosis of mania but did not apply other *DSM-III* exclusions. Because of the two-stage sampling design, subjects identified as having a lifetime disorder also had active depressive symptoms at the index visit, but they did not necessarily meet *DSM-III* criteria for current depressive disorder. There were 1,152 patients who met our definition of lifetime depressive disorder.

We developed an indicator of having current depressive disorder among patients with a lifetime depressive disorder as a covariate in our analyses. Current depression was defined as having, in addition to a lifetime disorder, 1) an episode of either major depression or dysthymia within the past 12 months, and 2) no remission (i.e., 2 months or more with two or fewer symptoms of depression, according to the criteria of Keller et al. [54], since the onset of the recent episode).

The data elicited by the Patient Screener on age, sex, race, employment, and marital status were also included as covariates in the analyses.

Type of Specialty/Type of Payment for Services

Medical specialty was determined from American Medical Association subspecialty society lists and the telephone screening of clinicians. Specialty was dichotomized as general medical provider versus mental health specialist.

Type of payment for services (prepaid versus fee-for-service) was determined by the system from which the patient was sampled and by items in the Patient Screener and second-stage telephone interview about insurance coverage. We grouped together all patients in prepaid plans, whether they received care in an HMO, group practice, or the solo/single-specialty group sector, and all patients in fee-for-service plans, whether they were in a group practice or the solo/single-specialty group sector.

Diagnosis of Chronic Medical Conditions (Dependent Variables)

The definitions of eight chronic medical conditions are given in appendix 1. Each condition was assessed as part of the initial screening of patients in clinicians' offices by using one or two items on the Patient Screener requiring a yes or no response. Data on arthritis and

diabetes were obtained on both versions of the Patient Screener and thus are available for all 1,152 depressed patients. Data on the other six conditions, however, were collected on one version of the Patient Screener and are thus available for only 572 depressed patients (a random subsample).

We used data from the Patient Screener as indicators of severity of hypertension and diabetes: information on the number of medications currently being taken for hypertension and whether the person was currently taking insulin.

For all patients, at the end of the visit during which patients were screened, the treating clinician was asked to indicate whether the patient had diabetes and was currently taking insulin and whether the patient had hypertension. In addition, for a subsample of patients (those who were enrolled in a 2-year longitudinal follow-up study), the presence or absence of medical conditions was assessed through a structured medical interview and physical examination conducted shortly after enrollment by study clinicians (independent of the treating provider).

Because some treating mental health specialists had a relatively high rate of missing data on presence or absence of medical conditions and because the more detailed study interview/examination data were available only on the longitudinal study subsample, we relied on the patient self-report data. As a partial test of the validity of this approach, we compared responses from different sources of information (patient, treating doctor, study staff interview) for all patients with multiple sources of data. Agreement among data sources was moderate to excellent. For example, for the 233 patients in the longitudinal study who indicated on the Patient Screener that they were taking insulin and participated in the physical examination, the study's independent clinician agreed that 220 (94%) had insulin-dependent diabetes. For the 217 patients who reported on the Patient Screener that they had a myocardial infarction and participated in the physical examination, the independent study clinician confirmed the diagnosis for 203 (94%). For the 815 patients reporting hypertension on the Patient Screener and participating in the physical examination, the study clinician confirmed the diagnosis for 774 (95%). For the 3,616 patients reporting hypertension on the Patient Screener (but who did not necessarily complete the physical examination), the treating clinician confirmed the diagnosis for 2,469 (68%). Thus, there was evidence of reasonable validity of the patient self-report for the more serious medical conditions on which we had multiple sources of data.

Statistical Methods

We used multiple regression techniques to estimate the effect of type of treatment provider (general medical versus mental health specialty) and type of payment (prepaid versus fee-for-service) on the likelihood of a depressed patient having each medical condition, any medical condition, and the total number of medical

conditions. For dichotomous variables (each medical condition and any condition) we used multiple logistic regression; for continuous variables (counts) we used multiple linear regression. The covariates for each regression were gender, age, employment, marital status, race, study site, and presence or absence of a current depressive disorder. We also tested terms for interactions between type of payment, type of provider, and presence of current depressive disorder. Unless otherwise stated, data were weighted for probability of response by the treating clinician and probability of response on the telephone interview by patients.

Using estimates from the regression models, we generated predictions of the likelihood of having a comorbid condition, the number of comorbid conditions, etc., for different patient groups. These predictions were adjusted for all covariates in the model. To draw inferences, we examined the *t* tests for the regression coefficients for type of provider and type of payment.

Because there were only one to two patients, on average, per treating provider, any adjustment of the standard errors or inference statistics for the clustered sampling design (of patients nested within providers) is trivial. We conducted analyses in which we formally corrected our estimates, confirming that the adjustments were minor. For example, standard errors required adjusting by only 1%–5%. Here, we present uncorrected standard errors and inference statistics.

RESULTS

Table 1 presents the demographic characteristics (based on unweighted data) of the 1,152 participants with lifetime depressive disorder by specialty of the treating clinician and by type of payment for services. Depressed patients visiting mental health specialists were younger and more likely to be white than were depressed patients visiting medical clinicians. Depressed patients receiving fee-for-service care were older, more likely to be female, and less likely to be employed and to be nonwhite than were depressed patients receiving prepaid care (table 1).

Table 2 presents the predicted (adjusted) percentage of patients with lifetime depression who had any and each medical condition, estimated from the multiple regression models. The sample sizes for the predictions were either 572 or 1,152, depending on whether data were available from one or both versions of the Patient Screener. As shown in table 2, there were no significant differences among depressed patients at the $p < 0.05$ level by type of payment in the prevalence of having any chronic medical condition or of having any of the specific conditions.

Table 2 also indicates that there was no significant difference in the prevalence of having any chronic medical condition, other factors being equal, for depressed patients who were treated by mental health specialists versus general medical providers. The adjusted prevalences of hypertension and arthritis were greater among

TABLE 1. Demographic Characteristics of 1,152 Patients With Lifetime Depressive Disorder, by Type of Provider and Payment (Unweighted Data)

Characteristic	Provider		Payment	
	Medical	Mental Health	Fee-for-Service	Prepaid
Male				
Sample size	663	489	574	578
N	161	142	135	168
%	24.3	29.0	23.5 ^a	29.1
Married				
Sample size	651	486	569	568
N	292	205	260	237
%	44.9	42.2	45.7	41.7
Employed				
Sample size	635	478	557	556
N	388	319	316	391
%	61.1	66.7	56.7 ^b	70.3
Nonwhite				
Sample size	647	480	568	559
N	184	50	77	157
%	28.4 ^c	10.4	13.6 ^d	28.1
Age (years)				
Sample size	662	489	573	578
Mean	44.1 ^e	39.3	43.0 ^f	41.1
SD	15.5	11.1	13.8	12.9

^aRegression coefficient $t=2.14$, $df=1,150$, $p<0.05$.

^bRegression coefficient $t=4.75$, $df=1,111$, $p<0.0001$.

^cRegression coefficient $t=7.56$, $df=1,125$, $p<0.0001$.

^dRegression coefficient $t=6.11$, $df=1,125$, $p<0.0001$.

^eRegression coefficient $t=6.07$, $df=1,149$, $p<0.0001$.

^fRegression coefficient $t=2.39$, $df=1,149$, $p<0.05$.

patients of general medical clinicians than among patients of mental health specialists (table 2).

We were concerned that the relatively high prevalence of hypertension in medical practices could be largely due to the particular medical subspecialists (cardiologists and endocrinologists) included in our provider sample. We conducted an analysis excluding patients of these subspecialists. The results were virtually identical to those reported for all of the medical clinicians.

We used multiple regression analyses and the general linear model to estimate the log-transformed mean number of chronic medical conditions among depressed patients with any chronic medical condition. Other factors being equal, medically ill depressed patients of mental health specialists had 1.8 comorbid chronic medical conditions, while similar patients of medical clinicians had 1.6 conditions. The regression coefficient representing this effect (the interaction of specialty and having any medical condition in predicting the number of conditions) was significant ($t=2.66$, $df=534$, $p<0.01$).

As shown in table 3, among patients with depressive disorder and hypertension, those visiting medical clinicians were significantly more likely than those visiting mental health specialists to be taking antihypertensive medications (after we adjusted for other factors). Among patients with depressive disorder and diabetes, those visiting medical clinicians were more likely than those visiting mental health specialists to have insulin-dependent diabetes, other factors being equal. We reached similar conclusions about hypertension in a sensitivity analysis comparing patients of mental health specialists and pa-

TABLE 2. Predicted (Adjusted) Percentage of Patients With Lifetime Depressive Disorder Who Had a Chronic Medical Condition, by Type of Provider and Payment^a

Medical Condition	Provider				Payment			
	Medical (N=663)		Mental Health (N=489)		Fee-for-Service (N=574)		Prepaid (N=578)	
	%	SE	%	SE	%	SE	%	SE
Any medical condition	71.0	2.7	64.9	2.8	69.0	2.7	66.9	2.7
Advanced coronary artery disease	5.5	1.2	3.2	1.7	4.9	1.4	5.0	1.6
Hypertension	43.1 ^b	3.1	24.4	3.1	37.1	3.1	33.0	2.9
Diabetes	13.4	1.4	9.8	1.6	11.3	1.4	13.1	1.5
Gastrointestinal disorder	11.4	2.0	16.6	2.7	16.0	2.5	10.6	1.9
Chronic back problems	9.8	1.9	8.8	1.9	8.4	1.9	10.5	1.9
Chronic lung problems	18.8	2.7	12.8	2.5	16.1	2.6	16.3	2.4
Angina only	3.3	1.0	4.6	1.5	5.5	1.5	2.1	0.8
Arthritis	26.2 ^c	1.7	20.3	2.0	24.0	1.8	24.4	1.7

^aAdjusted for age, sex, marital and employment status, race, and presence of current depressive disorder. The sample size for the analysis is 1,152 for arthritis and diabetes (75 of these had missing data) and 572 for the other conditions (35 of these had missing data).

^bRegression coefficient $t=-4.10$, $df=534$, $p<0.0001$.

^cRegression coefficient $t=-2.21$, $df=1,076$, $p<0.05$.

tients of general medical clinicians (excluding cardiologists and endocrinologists). However, in these analyses, the magnitude of the difference in the severity of diabetes was smaller by one-third and was not significant at the 0.05 level.

There were no significant interactions between type of payment and type of provider or between presence or absence of a current depressive disorder and either the type of payment or the type of provider in predicting any indicator of extent or severity of medical comorbidity among the depressed patients.

These findings are based on a consecutive sample of patient visits, which overrepresents individuals with more than one visit, who tend to be more ill. To determine whether we would reach the same conclusions in a sample obtained over a longer time period, we conducted sensitivity analyses in which we weighted the data by the inverse of the number of health care visits in the previous 2 weeks (i.e., overweighting less frequent visitors). In these analyses, we reached the same conclusions, except there was also a tendency for depressed patients with fee-for-service coverage to have a higher prevalence of angina than similar patients with prepaid financing ($t=-2.14$, $df=519$). The specialty differences reported here were also reduced somewhat in magnitude but remained significant.

As a context for our findings, we used data from the Los Angeles project of the NIMH Epidemiologic Catchment Area Program (ECA) to estimate the prevalence of four chronic conditions in a general household adult sample consisting of Mexican-Americans and non-Hispanic whites. The design of the ECA and of the Los Angeles project are described in detail elsewhere (55–57). The measures of chronic medical conditions were respondents' self-reports of ever having the condition and of currently having the condition (8, 26). For each condition, we used the same time frame as defined in appendix 1. The ECA household estimates were sex and age-adjusted to the Medical Outcomes Study lifetime depressed patient sample by using a direct method. The

TABLE 3. Predicted (Adjusted) Percentage of Patients With Lifetime Depressive Disorder Who Had Severe Hypertension or Diabetes, by Type of Provider

Patient Group	Provider			
	Medical		Mental Health	
	%	SE	%	SE
Patients taking any antihypertensive medication for hypertension (N=220)	54.7 ^a	4.2	36.9	5.9
Patients taking insulin injections for diabetes (N=333)	14.2 ^b	2.5	2.0	1.4

^aRegression coefficient $t=-2.44$, $df=219$, $p<0.05$.

^bRegression coefficient $t=-2.72$, $df=332$, $p<0.01$.

adjusted prevalence rates and the standard errors for the ECA household sample were 21.9%±0.8% for lifetime hypertension, 6.9%±0.5% for lifetime diabetes, 5.0%±0.4% for current chronic lung problems, and 17.7%±0.8% for current arthritis.

DISCUSSION

We provided estimates of how medical comorbidity of depressed patients differs across types of health care settings. We found evidence for a higher prevalence of hypertension and arthritis among depressed patients visiting general medical settings than among those visiting mental health specialty settings. We also found evidence for relatively more severe hypertension, as indicated by a higher probability of treatment with antihypertensive medication, among the general medical sector patients. The latter finding, however, could reflect either a true difference in severity or a difference in detection and treatment of hypertension. These findings are consistent with known differences in patterns of utilization (e.g., that physically ill patients are more likely to receive general medical care) and in the clinical

roles of mental health specialists and general medical clinicians (medical clinicians are more oriented toward treatment of physical illnesses).

We also found, however, that the differences in extent of medical comorbidity across the two provider sectors were not as great as one might expect. There was a similarly high prevalence (over 60%) of having any medical condition in both types of practice settings. The mean number of chronic medical conditions among those with any such condition, although somewhat higher in general medical practices, was about 2 for both types of practices. This suggests that the average management problem facing the clinician, in any setting, is diagnosing and treating depression in the context of multiple medical comorbidity. This conclusion emphasizes the importance of understanding the treatment implications of depression comorbid with medical illness. Only a few clinical studies have examined the efficacy of treatments for depression in the context of specific medical illnesses that are common in depressed patients (58). At least one study noted problems in completing the outcome study due to side effects of antidepressant medication in medically ill patients (18, 19). Although the issue of psychiatric-medical comorbidity has largely been the domain of the consultation-liaison psychiatrist in the context of recommending treatment for medical inpatients and outpatients (1), our findings suggest that this should become the orientation of clinicians in approaching the typical depressed adult outpatient in either the general medical or mental health specialty sector.

This conclusion is further enhanced by our null findings regarding differences by type of payment for services. We found neither a main effect of type of payment nor an interaction between type of payment and specialty sector in predicting level of medical comorbidity of depressed patients. Thus, the main conclusion that the average depressed patient is likely to have a comorbid medical illness applies across both prepaid and fee-for-service practices. On the basis of these findings, one would expect health care delivery systems that rely on different mixes of mental health specialists and general medical providers to differ somewhat in comorbidity of depressive and medical illnesses, but one would not necessarily expect differences in such comorbidity based on the degree of reliance on prepayment or fee-for-service financing.

For four of the conditions on which we had comparable data from a household sample, we found similar or higher prevalences of the medical conditions among the depressed patient samples, especially those visiting general medical providers, than among the household sample, even after sex and age adjustment. The mental health specialty patients with lifetime depression had a similar prevalence of hypertension and arthritis, a 50% greater prevalence of diabetes, and a 100% greater prevalence of chronic lung disease than did the household sample. The general medical patients with lifetime depression had roughly twice the prevalence of hypertension and diabetes, about one-third greater prevalence of arthritis, and over three times the prevalence of

chronic lung disease as the household sample. These findings are consistent with the conclusions of previous studies that there is a strong association between depression and chronic medical conditions (1-11). Because of the cross-sectional and observational design, however, we cannot use these data to comment on the causal nature of the relationship between depressive disorder and chronic medical conditions. For a patient sample, such as the Medical Outcomes Study sample, these associations could also reflect the effects of depression and chronic medical conditions on the decision to obtain care.

How valid are the measures of depression and medical illnesses on which our conclusions are based? Burke (59), in a comprehensive review, indicated that the DIS, while having certain known limitations in reliability and validity, is currently the most appropriate standardized psychiatric interview for purposes of large-scale research, such as that conducted here. Further, although we administered the DIS by telephone, we previously determined that route of administration (whether telephone or face-to-face) does not appear to affect the validity of assessment of lifetime depressive disorders (52). One important limitation of our conclusions is the reliance on patient self-report of chronic medical conditions. However, there is currently no established gold standard measure (in terms of reliability and validity) for assessing a comprehensive range of chronic medical conditions, especially in the context of depressive illness, although some conceptual frameworks have been proposed (39). For purposes of commenting on the extent of medical comorbidity in different health care systems, it was important to assess a broad spectrum of diseases, as we have done here, rather than examining one or two diseases in more clinical detail. Further, there is now increasing interest in assessing health status from the perspective of the patient's report (60). Because of this emphasis on self-report, however, one can appropriately interpret some of the conditions studied here, such as arthritis and back pain, as patient complaints. Nevertheless, such patient-reported conditions and complaints are highly predictive of use of both general medical and mental health care services and thus of considerable policy and clinical interest in their own right (61, 62). Further, we found relatively high agreement between patient reports of these conditions and reports by the treating providers and independent clinical assessments by study staff. Thus, although our approach to assessing medical conditions is derived from a general population survey tradition rather than a clinical research tradition, we think our data are sufficiently valid for the purposes addressed here.

Several important general limitations of the Medical Outcomes Study data and design were discussed by Tarlov et al. (50) and Wells et al. (51). They include 1) the reliance on data from select HMOs and group practices in specific urban U.S. sites (the conclusions may not generalize to other settings), 2) moderate clinician response rates, especially among solo/single-specialty group clinicians (but we found little evidence for either

patient or clinician nonresponse bias relevant to depression), and 3) the sampling design, which represents the typical office visit rather than the typical patient ever visiting a clinician and slightly overrepresents patients visiting small-volume practices. The consecutive sampling design could lead to high estimates of prevalence of comorbid medical conditions because patients with multiple consecutive visits tend to be sicker. Such patients are of particular clinical and policy interest, however. Moreover, we reached the same overall conclusions when we weighted the data to overrepresent patients who visited less frequently.

In sum, our data suggest that clinicians in all health care settings must be prepared to encounter chronic medical conditions and complaints in the depressed patients who visit them. On the basis of previous studies (9, 16–18), this medical comorbidity would be expected to complicate the assessment and management of the depression and the medical illness. We have not directly addressed these implications here, however. The “burden” of managing depression in the context of medical comorbidity may be somewhat greater for specific conditions in the general medical sector than in the mental health specialty sector, but the difference is not very great. From a public health perspective, the clinical management of depression needs to be reconceptualized by all providers as largely a problem of managing depression in the presence of medical illness. The importance of accomplishing this reorientation for the average practicing psychiatrist is further reinforced by recent research findings suggesting that mental health specialists tend to underdiagnose medical illnesses in their patients with serious psychiatric illnesses (40) and that both depression and serious medical illnesses independently contribute to the problems patients have in their daily functioning (51).

ACKNOWLEDGMENTS

Individuals who provided invaluable assistance include Linda Aiken and Alan Cohen of the Robert Wood Johnson Foundation, Barbara Keherer and Alvin Tarlov of the Henry J. Kaiser Foundation, Rebecca Rimal and Roseanne Siegel of the Pew Charitable Trust, David Larson of NIMH, and Al Williams and Ann Cianciolo of the RAND Corporation. The authors also thank Meenu Sandhu and Patti Camp for programming.

Cooperation and assistance in recruiting physicians and patients were provided by the American College of Physicians, the American Academy of Family Physicians, the American Academy of Pediatrics, APA, the American Psychological Association, and their local chapters in the study sites. The Medical Outcomes Study Liaison Committee representing these organizations consisted of Boris Astrachan, Steven Sharfstein, Harold Pincus, Gary VandenBos, Robert McGinnis, Claudene Clinton, Robert Haggerty, Gretchen Fleming, Boy Frame, Robert Moser, and Alvin Tarlov (chair).

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APPENDIX 1. Definitions of Patient-Reported Chronic Medical Conditions

Hypertension: patient was told by a doctor, nurse, or other health care professional that he or she has high blood pressure or hypertension.

Diabetes: patient was told by a doctor, nurse, or other health care professional that he or she has high blood sugar or diabetes.

Advanced coronary artery disease: patient was told by a doctor or other health care professional that he or she had a heart attack, myocardial infarction, or coronary and reports that it occurred within the last 12 months; or the patient reports having heart failure or enlarged heart (with or without angina).

Angina: patient reports now having angina but did not recently have a myocardial infarction or heart failure.

Arthritis: patient reports now having arthritis.

Back problems: patient reports now having back problems, including disk or spine problems.

Lung problems: patient reports now having asthma or other severe lung problems, such as chronic bronchitis and emphysema.

Gastrointestinal disorder: patient reports now having ulcer (duodenal, stomach, or peptic) or chronic inflamed bowel, enteritis, or colitis.

New Methods in Cross-Cultural Psychiatry: Psychiatric Illness in Taiwan and the United States

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Objective: Cross-cultural psychiatric research has suffered from many methodological shortcomings. To answer some of these shortcomings, the present study compared rates of psychiatric disorders in Taiwan and the United States by combining data from both countries into a single data set. **Method:** Results from large, community-based surveys in the United States and Taiwan, the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area survey and the Taiwan Psychiatric Epidemiological Project, were combined into a single data set. This integration of the data sets was possible because both surveys used the NIMH Diagnostic Interview Schedule to ascertain cases. The integrated data sets were then analyzed with identical algorithms to generate lifetime prevalence rates of psychiatric disorders according to DSM-III criteria for both the United States and Taiwan. **Results:** Lifetime prevalence rates of psychiatric illness in Taiwan were generally lower than U.S. rates. The rates of any disorder were 21.56% in Taiwan and 35.55% in the United States ($Z=22.34$, $p<10^{-109}$). The rates of most specific disorders were lower in Taiwan, and none of the rates was higher in Taiwan. **Conclusions:** While a culturally determined response bias may have lowered the rates in Taiwan somewhat, the results appear to be valid. Implications for the future use of structured diagnostic interviews in cross-cultural research are discussed.

(Am J Psychiatry 1991; 148:1697-1704)

Historically, cross-cultural epidemiological studies in psychiatry have suffered from several problems (1). First, case identification techniques varied from site to site or were not described fully. In many early studies, methods were not standardized across cultures. Second, only one diagnosis was studied, or a global impression of psychiatric illness was given without an attempt to make specific diagnoses. Few large cross-cultural studies have compared a range of specific psychiatric illnesses. Third, even when standardized methodologies were used, study populations were drawn from clinics or hospitals and so represented skewed samples of the populations being compared.

Despite these difficulties, a few studies stand out as landmarks in cross-cultural psychiatry. The United States-United Kingdom Diagnostic Project was one (2).

In that study, identical diagnostic methods were applied in different countries. A single team of investigators interviewed patients on both sides of the Atlantic with standardized interviews. This was possible because few language and cultural barriers separate the United States and the United Kingdom.

A second important set of studies were the International Pilot Study of Schizophrenia (3) and the World Health Organization Collaborative Study on Determinants of Outcome of Severe Mental Disorders (4). In those studies, researchers used similar sampling methods in multiple study sites and a standardized diagnostic instrument, the Present State Examination (5).

A recent trend has made possible a new type of cross-cultural study. The advent of precise diagnostic criteria and highly structured interviews has allowed nonclinicians to make diagnoses with a reasonable degree of reliability and validity. These interviews have been used across various cultures in general population community surveys. The present paper is an attempt to make cross-cultural comparisons by taking advantage of two general population surveys that used the same diagnostic instrument in translation.

In this study we compare data from the National Institute of Mental Health (NIMH) Epidemiologic Catchment

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TABLE 1. Lifetime Prevalence Rates of Major Psychiatric Disorders in Taiwan and the United States

DSM-III Diagnosis	Taiwan			United States			Z	p
	Unweighted Affected N	%	SE	Unweighted Affected N	%	SE		
Any diagnosis	2,365	21.56	0.39	6,888	35.55	0.49	22.34	<10 ⁻¹⁰⁹
Major depression	125	1.14	0.10	857	5.15	0.23	15.99	<10 ⁻⁵⁶
Dysthymic disorder	182	1.66	0.12	614	3.26	0.18	7.40	<10 ⁻¹²
Manic disorder	19	0.17	0.04	62	0.37	0.06	2.77	0.006
Alcohol abuse/dependence	758	7.18	0.25	2,075	13.43	0.35	14.53	<10 ⁻⁴⁷
Drug abuse/dependence	17	0.16	0.04	876	6.12	0.25	23.54	<10 ⁻¹²¹
Antisocial personality disorder	20	0.18	0.04	365	2.53	0.16	14.25	<10 ⁻⁴⁵
Cognitive impairment	420	3.85	0.18	1,563	4.72	0.22	3.06	0.002
Schizophrenia	29	0.27	0.05	170	0.98	0.10	6.35	<10 ⁻⁹
Schizophreniform disorder	4	0.04	0.02	20	0.11	0.03	1.94	0.05
Generalized anxiety disorder ^a	770	7.75	0.27	652	8.44	0.42	1.38	0.17
Panic disorder	40	0.37	0.06	254	1.56	0.13	8.31	<10 ⁻¹⁶
Phobic disorder	507	4.64	0.20	2,721	12.53	0.34	20.00	<10 ⁻⁸⁸
Obsessive-compulsive disorder	81	0.74	0.08	462	2.54	0.16	10.06	<10 ⁻²³
Somatization disorder	9	0.08	0.03	44	0.12	0.04	0.80	0.42

^aU.S. data from seven catchment areas only.

Area (ECA) survey (6) and the Taiwan Psychiatric Epidemiological Project (7). Both of these studies used versions of the NIMH Diagnostic Interview Schedule (DIS) (8) to identify psychiatric cases. By combining DIS results from both countries into a single data bank, we could apply the same diagnostic criteria and identical analyses, thus allowing a detailed comparison of patterns of psychiatric illness. Moreover, variation in results due to use of different analytic techniques is avoided. We have not limited ourselves to a single diagnosis and have examined a broad spectrum of psychiatric illnesses. In addition, to avoid biases inherent in studying clinical cases, both studies used general population samples.

METHOD

The ECA survey was a general population study conducted in the early 1980s at five sites (with 12 catchment areas among those five sites) across the United States (6). The ECA survey used the DIS to identify psychiatric cases (8). For this study, diagnoses were based on *DSM-III* criteria. The diagnostic categories covered are shown in table 1.

The specific sampling procedures in the ECA survey were complex and varied somewhat among the sites. They have been described in detail elsewhere (8). The multistaged, clustered design of the sampling plan, along with the intentional oversampling of important subpopulations at some sites of the ECA survey, necessitated statistical weighting of each case for proper analysis of the sample as a whole. All cases from the United States were weighted by standardizing to the catchment area census data. Standardizing was performed on the basis of age, gender, and race/ethnicity. All results described here take into account this weighting in determining the rates of the various illnesses for the general population in each of the catchment areas. In order to make the sampling frames most comparable, ECA data in this study include the community sam-

ples and exclude institutionalized samples because no institutions were sampled in Taiwan. The total sample size was 18,320.

The Taiwan study used a Chinese Mandarin translation of version 2 of the DIS completed in 1979. The translator (H.-G.H.) had completed the 4-year residency program in the Department of Psychiatry, National Taiwan University, and, at the time he wrote the original translation, was completing a 3-year residency training program in the Department of Psychiatry at Washington University. His training in these institutions included an emphasis on sociocultural psychiatry and psychiatric diagnosis. He was, therefore, uniquely situated to comprehend the meaning of the DIS symptom questions and to produce an equivalent Chinese Mandarin version (DIS-CM).

Certain modifications of the DIS were necessary in the creation of the DIS-CM because of cultural and language differences between the United States and Taiwan. Overall, the modifications of the DIS were thought to be minor in their possible interference with comparability of data and they were considered necessary in applying the DIS to Taiwan.

A Mandarin-to-English back translation by another translator was also done and was reviewed by Professor Lee Robins, one of the original authors of the DIS. She corrected several symptom questions, and the Chinese version was similarly corrected.

An interrater reliability study of the DIS-CM found reliability to be satisfactory (7). Further revisions of the DIS-CM improved the items of poor reliability and incorporated revisions of the English version of the DIS (i.e., DIS version 3).

Validity of the Chinese instrument was studied by comparing diagnoses derived from the DIS-CM when given by a paramedical interviewer with a psychiatrist's diagnoses based on *DSM-III* criteria (9). Overall, the results confirmed that the DIS-CM was valid as a psychiatric epidemiological tool for use in the Taiwan Psychiatric Epidemiological Project.

The design of the Taiwan Psychiatric Epidemiological Project study closely resembled that of the ECA survey. In both, nonclinicians administered a highly structured interview in a community-based survey designed to ascertain the prevalence of the major psychiatric disorders and associated health care utilization. Researchers used the DIS-CM to identify psychiatric cases, just as the DIS was used in the ECA survey. Overall, 11,004 respondents were interviewed at three sites: metropolitan Taipei, small towns outside Taipei, and rural villages distant from Taipei. These were chosen to represent a broad sociodemographic cross-section of the population. Sampling was of considerable complexity and involved a multistage random selection of respondents from a complete listing of domiciles (10). This provided a random sample of the total household population in each of the communities, so no weighting of data was necessary during statistical analysis.

For purposes of flow, wording and ordering of questions varied between the DIS and the DIS-CM but remained nearly identical across the five ECA sites (8) and the three Taiwan sites (10). Dr. Lee Robins and her colleagues in St. Louis trained investigators from the five ECA sites in the use of the DIS (8). This helped to ensure the comparability of interviewer training. Similarly, the primary investigators of the Taiwan project undertook the same training course in St. Louis and supervised interviewer training in Taiwan.

Completion rates were similar for the ECA survey and the Taiwan Psychiatric Epidemiological Project. The response rate in Taiwan was 75% (11,004 recorded interviews from attempted interviews with a prepared sample actually drawn of 14,729), close to the 75%–80% rate recorded across ECA sites. Furthermore, both surveys reported interview completion rates close to 100% for interviews that were initiated.

Data preparation included manipulating Taiwan project data into the ECA format. For this purpose a data tape was sent to St. Louis from Taiwan. The data sets were integrated, and then a data error checking and cleaning program probed for illogical and inconsistent data (e.g., disallowed skip sequences and out of range response codes). Recodes became necessary because of coding differences between the Taiwan project and the ECA survey. During this time researchers from Taiwan came to St. Louis to assist in data preparation and analysis. Their input was critical to resolve minor differences in data coding and ordering of questions. Some of the few DIS items not present in the DIS-CM could be inferred from the rest of the DIS-CM; otherwise, they were coded as missing. This extensive data cleaning generally brought the DIS-CM data into conformity with the DIS data. After all cleaning procedures were completed, the final error rate in response coding of the Taiwan project data represented 0.2% of total responses. Although somewhat higher than that of the ECA data sets, this error rate was acceptably low.

Analysis of the Taiwan Psychiatric Epidemiological

Project was first performed in Taiwan with a Fortran computer algorithm, and results have been presented elsewhere (10). Analysis of the combined ECA survey-Taiwan project data was performed in the present study with the computer algorithms developed for the ECA survey (8). Identical SAS algorithms were applied to both the Taiwan project and the ECA data sets. Lifetime diagnostic prevalence rates were computed for the combined Taiwan sites and for the combined U.S. sites. In addition, diagnostic rates were computed for the three individual Taiwan sites of the Taiwan project and for the 12 U.S. catchment areas of the ECA survey. Standard errors of the Taiwan rates were calculated with the binomial distribution. Standard errors of the U.S. rates were calculated, taking account of the sampling weights.

A comparison of the present analysis of Taiwan Psychiatric Epidemiological Project and ECA survey data with those of the original analyses (10, 11) revealed small differences. The rates of the psychiatric disorders in the ECA survey were identical to the originally reported rates, as expected, because the present analysis used the ECA survey data and methods. On the other hand, certain differences were found from the reported rates of disorders in Taiwan (10). The rates of cognitive impairment and generalized anxiety disorder were higher in the present study than in the original analyses because of differences in the handling of missing or incorrect responses. Minor differences in some other rates arose from the diagnosis-specific population bases employed. The present analyses excluded from the base for each diagnosis any respondent whose diagnosis was doubtful because of incorrect or missing responses. In contrast, the original analysis of the Taiwan project data retained all respondents in the base for each diagnosis.

The differences in lifetime prevalence rates of 14 psychiatric diagnoses between the combined Taiwan and the combined U.S. sites were analyzed with two-tailed normal (*Z*) tests based on the differences in the rates and the estimated standard errors of the rates. These results are presented in table 1. Similarly, the lifetime prevalence rate of each psychiatric diagnosis at each of the three Taiwan locations was compared with the rate at each of the 12 U.S. catchment areas; the results are presented in tables 2–4.

The *p* values are presented for each of the comparisons in table 1. Because of the large number of comparisons (*N*=15), some multiple-comparison correction, such as the Bonferroni (12), should be employed when assessing statistical significance. To save space, actual *p* values are not used in tables 2–4. Instead, symbols are used to indicate *p* values less than 0.01 or 0.001. These unusually stringent significance levels correspond to Bonferroni corrections of five and 50 multiple comparisons at the 0.05 significance level and will be of assistance in scanning the table for patterns. In the discussion of tables 2–4, a difference with a *p* value less than 0.001 will be described as significant. A difference with a *p* value less than 0.01 but greater than 0.001 will be described as possibly significant.

TABLE 2. Lifetime Prevalence Rates of DSM-III Major Depression, Dysthymic Disorder, and Generalized Anxiety Disorder in Taiwan and U.S. Communities

Site	Major Depression			Dysthymic Disorder			Generalized Anxiety Disorder		
	Unweighted Sample N	%	SE	Unweighted Sample N	%	SE	Unweighted Sample N	%	SE
Metropolitan Taipei	4,997	0.94	0.14	4,997	1.42	0.17	4,278	4.72	0.32
Small Taiwan towns	2,981	1.61	0.23	2,981	2.28	0.27	2,852	11.64	0.60
Rural Taiwan villages	2,964	1.01	0.18	2,964	1.45	0.22	2,803	8.42	0.52
Western New Haven	3,434	5.48	0.51 ^{a,b,c}	3,430	3.23	0.40 ^{a,c}	—	—	—
Central New Haven	1,465	5.99	0.83 ^{a,b,c}	1,465	3.09	0.61 ^d	—	—	—
Johns Hopkins Hospital catchment area	859	3.18	0.68 ^{d,e}	859	2.00	0.54	—	—	—
Baltimore City Hospital catchment area	1,087	3.30	0.62 ^{a,c}	1,088	2.39	0.53	—	—	—
Central Baltimore	1,292	3.57	0.58 ^{a,c,f}	1,292	1.87	0.42	—	—	—
Downtown St. Louis	973	5.80	1.34 ^{a,c,f}	972	4.94	1.24 ^{d,e}	786	8.64	1.76
Suburban St. Louis	1,262	4.75	0.84 ^{a,b,c}	1,262	4.53	0.82 ^{a,c,f}	1,075	8.61	1.20 ^d
Rural Missouri	736	4.95	0.81 ^{a,b,c}	736	2.74	0.61	623	9.16	1.16 ^a
Urban North Carolina	1,881	5.13	0.62 ^{a,b,c}	1,882	2.39	0.43	1,464	10.43	0.98 ^a
Rural North Carolina	1,943	2.44	0.49 ^d	1,943	2.03	0.44	1,611	7.66	0.93 ^{b,d}
East Los Angeles	1,377	4.13	0.62 ^{a,b,c}	1,377	3.91	0.61 ^{a,c}	984	5.15	0.81 ^{b,c}
Western Los Angeles	1,739	7.03	0.68 ^{a,b,c}	1,739	4.44	0.54 ^{a,b,c}	1,409	8.39	0.81 ^{a,f}

^aMetropolitan Taipei versus U.S. sites: $Z > 3.29$, $p < 0.001$.^bSmall Taiwan towns versus U.S. sites: $Z > 3.29$, $p < 0.001$.^cRural Taiwan villages versus U.S. sites: $Z > 3.29$, $p < 0.001$.^dMetropolitan Taipei versus U.S. sites: $Z > 2.58$, $p < 0.01$.^eRural Taiwan villages versus U.S. sites: $Z > 2.58$, $p < 0.01$.^fSmall Taiwan towns versus U.S. sites: $Z > 2.58$, $p < 0.01$.

RESULTS

A comparison of Taiwan and U.S. lifetime prevalence rates of 14 psychiatric disorders and a combined "any diagnosis" is presented in table 1. The rate of any diagnosis for Taiwan was 21.56%; the rate for the United States was 35.55%. The rate for the United States is, if anything, an underestimate because it does not include diagnoses of generalized anxiety disorder in two of the five sites. Prevalence for all diagnoses was markedly lower in Taiwan than in the United States. After Bonferroni correction for multiple comparisons, all but four differences were statistically significant at or well beyond the 0.05 significance level. Three of the four differences not statistically significant were for low prevalence diagnoses—manic, schizophreniform, and somatization disorders. The fourth nonsignificant difference was for generalized anxiety disorder.

To examine lifetime prevalence rates in more detail, the rates of specific diagnoses at the three study sites in Taiwan were compared with those in the 12 U.S. catchment areas. By comparing rates of the individual sites, it can be determined whether any of the Taiwan sites had rates that were within the range of U.S. rates or were as much lower at the individual areas as the national rates would indicate.

Affective Disorders

The lifetime prevalence rates of major depression are presented in table 2. The rate of major depression in the three Taiwan sites was significantly lower than most U.S. rates. Even the rate in Taiwan's small towns, which was the highest rate in Taiwan, was significantly lower

than the rate in seven U.S. catchment areas and possibly significantly lower than that in two additional catchment areas.

The rate of dysthymic disorder in Taiwan's small towns (the highest in Taiwan) was well within the range of U.S. values, as shown in table 2. The rates in Taipei and Taiwan's rural villages were lower than all U.S. rates but often not significantly so.

For manic episodes, a rare diagnosis in both countries, there was no significant difference among the rates at any individual areas. The Taiwan rates ranged from 0.13% to 0.20%, and the U.S. rates ranged from 0% to 0.66%.

Schizophrenic Disorders

The rates of schizophrenia (table 3) were lower at all of the Taiwan sites than at any of the U.S. areas, but the difference was not statistically significant for most comparisons.

For schizophreniform disorder there was no significant difference among the rates at any individual areas. The rates were all quite low and ranged from 0.02% to 0.07% in Taiwan and from 0% to 0.34% in the United States.

Anxiety Disorders

U.S. data for generalized anxiety disorder (table 2) are available for only seven catchment areas because the appropriate questions were added to the DIS after the New Haven and Baltimore surveys had been completed. The rates in Taiwan bracket the U.S. rates. The rate in Taiwan's small towns was higher, and the rate in Taipei

TABLE 3. Lifetime Prevalence Rates of DSM-III Alcohol Abuse or Dependence, Schizophrenia, and Cognitive Impairment in Taiwan and U.S. Communities

Site	Alcohol Abuse or Dependence			Schizophrenia			Cognitive Impairment		
	Unweighted Sample N	%	SE	Unweighted Sample N	%	SE	Unweighted Sample N	%	SE
Metropolitan Taipei	4,682	5.17	0.32	4,987	0.34	0.08	4,958	1.53	0.17
Small Taiwan towns	2,951	9.96	0.55	2,980	0.23	0.09	2,984	6.07	0.44
Rural Taiwan villages	2,929	7.58	0.49	2,965	0.17	0.08	2,966	5.50	0.42
Western New Haven	3,424	12.07	0.73 ^{a,b}	3,430	1.35	0.26 ^{a,b,c}	3,422	4.54	0.47 ^a
Central New Haven	1,460	10.07	1.06 ^a	1,465	1.59	0.44 ^{d,e,f}	1,462	3.30	0.63 ^{d,f}
Johns Hopkins Hospital catchment area	858	17.00	1.46 ^{a,b,c}	852	1.51	0.47 ^{e,f}	887	10.30	1.16 ^{a,b,c}
Baltimore City Hospital catchment area	1,080	15.53	1.26 ^{a,b,c}	1,077	1.16	0.37 ^f	1,140	6.16	0.82 ^a
Central Baltimore	1,289	11.75	1.01 ^{a,b}	1,290	1.09	0.33 ^f	1,357	3.07	0.53 ^{b,c,d}
Downtown St. Louis	970	19.68	2.28 ^{a,b,c}	969	1.45	0.68	980	11.70	1.83 ^{a,b,e}
Suburban St. Louis	1,255	15.92	1.44 ^{a,b,c}	1,258	0.65	0.32	1,260	4.77	0.84 ^a
Rural Missouri	733	13.90	1.29 ^{a,b,e}	735	0.37	0.22	736	2.59	0.59 ^{b,c}
Urban North Carolina	1,873	8.97	0.80 ^a	1,874	1.56	0.35 ^{a,b,c}	1,893	7.07	0.71 ^a
Rural North Carolina	1,938	9.60	0.93 ^a	1,938	1.21	0.35 ^{e,f}	1,947	12.26	1.03 ^{a,b,c}
East Los Angeles	1,366	15.81	1.14 ^{a,b,c}	1,373	0.41	0.20	1,373	7.86	0.84 ^a
Western Los Angeles	1,733	14.37	0.93 ^{a,b,c}	1,737	0.46	0.18	1,741	2.41	0.40 ^{b,c}

^aMetropolitan Taipei versus U.S. sites: $Z > 3.29$, $p < 0.001$.^bRural Taiwan villages versus U.S. sites: $Z > 3.29$, $p < 0.001$.^cSmall Taiwan towns versus U.S. sites: $Z > 3.29$, $p < 0.001$.^dMetropolitan Taipei versus U.S. sites: $Z > 2.58$, $p < 0.01$.^eSmall Taiwan towns versus U.S. sites: $Z > 2.58$, $p < 0.01$.^fRural Taiwan villages versus U.S. sites: $Z > 2.58$, $p < 0.01$.

lower, than every U.S. rate. The rate in Taiwan's rural villages was well within the range of U.S. rates.

The rates of panic disorder and phobic disorder are seen in table 4. In both cases the three Taiwan rates were lower than all the U.S. rates. Taiwan's small towns had the highest rate in Taiwan for both diagnoses. However, for many comparisons even this rate was significantly lower than the U.S. rates.

The rates of obsessive-compulsive disorder (table 4) at the Taiwan sites were lower than every U.S. rate. Even Taipei's rate, the highest in Taiwan, was significantly lower than rates in six U.S. areas.

For somatization disorder the rates were uniformly low, and there was no significant difference between the individual areas. The rates in Taiwan ranged from 0.04% to 0.13%, and the rates in the United States ranged from 0% to 0.58%.

Substance Use Disorders

For drug abuse and/or dependence the rates at all individual Taiwan sites were significantly lower than the rates at every U.S. area. The rates in Taiwan ranged from 0.03% to 0.27%; in the United States they ranged from 2.06% to 10.54%.

The rates of alcohol abuse and/or dependence in Taiwan ranged from 5.17% to 9.96% (table 3). The U.S. rates ranged from 8.97% to 19.68%. The rate in Taipei (Taiwan's lowest rate) was significantly lower than every U.S. rate. The rate in Taiwan's small towns (the highest rate in Taiwan) was not significantly different from the rates in five U.S. sites, was possibly significantly lower than the rate in one U.S. site, and was significantly lower than the rates in the other six U.S. sites.

The rate in rural Taiwan villages was significantly lower than rates in nine U.S. sites; it was not significantly lower than the rates in three sites. More detail concerning a comparison of rates of alcoholism can be found elsewhere (13-15).

Personality Disorder

The lifetime rate of antisocial personality disorder at each Taiwan site was significantly lower than the rate at every U.S. site. The Taiwan rates ranged from 0.10% to 0.22%. The U.S. rates ranged from 1.49% to 5.66%.

Cognitive Impairment

Rates of cognitive impairment in Taiwan's small towns and rural villages were well within the range of rates in the U.S. areas, as shown in table 3. The rates for Taiwan's small towns and rural villages were higher than six U.S. rates and lower than six. On the other hand, Taipei's rate (the lowest in Taiwan) was significantly lower than eight U.S. rates and possibly significantly lower than two additional rates.

DISCUSSION

The most important finding of our study is that rates of most of the psychiatric illnesses we studied are lower in Taiwan than in the United States. In considering these results, various approaches are possible. Methodological issues, cultural issues, and social issues can be examined for their possible roles in these cross-national similarities and differences (13).

TABLE 4. Lifetime Prevalence Rates of *DSM-III* Obsessive-Compulsive Disorder in Taiwan and U.S. Communities

Site	Obsessive-Compulsive Disorder			Panic Disorder			Phobic Disorder		
	Unweighted Sample N	%	SE	Unweighted Sample N	%	SE	Unweighted Sample N	%	SE
Metropolitan Taipei	4,979	1.02	0.14	4,979	0.30	0.08	4,980	4.56	0.30
Small Taiwan towns	2,979	0.70	0.15	2,990	0.57	0.14	2,983	5.90	0.43
Rural Taiwan villages	2,965	0.30	0.10	2,962	0.27	0.10	2,968	3.50	0.34
Western New Haven	3,424	2.57	0.36 ^{a,b,c}	3,438	1.52	0.27 ^{a,c,d}	3,437	8.41	0.62 ^{a,b,c}
Central New Haven	1,462	2.42	0.54 ^{c,d}	1,469	1.33	0.40	1,470	6.53	0.86 ^e
Johns Hopkins Hospital catchment area	857	2.62	0.62 ^{c,d}	856	1.38	0.45	858	30.22	1.78 ^{a,b,c}
Baltimore City Hospital catchment area	1,079	3.13	0.61 ^{a,b}	1,086	1.92	0.48 ^{a,c,d}	1,089	21.26	1.42 ^{a,b,c}
Central Baltimore	1,288	2.82	0.52 ^{a,b,c}	1,294	1.18	0.34	1,294	21.34	1.28 ^{a,b,c}
Downtown St. Louis	971	1.52	0.70	971	1.49	0.70	972	9.50	1.68 ^{c,f}
Suburban St. Louis	1,258	2.36	0.60 ^{c,d}	1,260	0.84	0.36	1,262	10.77	1.22 ^{a,b,c}
Rural Missouri	734	1.67	0.48 ^e	732	2.17	0.54 ^{a,c,d}	735	8.21	1.02 ^c
Urban North Carolina	1,871	3.38	0.50 ^{a,b,c}	1,883	1.82	0.37 ^{a,c,d}	1,882	21.60	1.15 ^{a,b,c}
Rural North Carolina	1,939	3.12	0.55 ^{a,b,c}	1,939	1.37	0.37 ^{e,f}	1,942	20.33	1.27 ^{a,b,c}
East Los Angeles	1,371	1.49	0.38 ^e	1,380	1.07	0.32	1,377	12.81	1.04 ^{a,b,c}
Western Los Angeles	1,738	2.58	0.42 ^{a,b,c}	1,738	1.75	0.35 ^{a,c,d}	1,738	10.65	0.81 ^{a,b,c}

^aMetropolitan Taipei versus U.S. sites: $Z > 3.29$, $p < 0.001$.

^bSmall Taiwan towns versus U.S. sites: $Z > 3.29$, $p < 0.001$.

^cRural Taiwan villages versus U.S. sites: $Z > 3.29$, $p < 0.001$.

^dSmall Taiwan towns versus U.S. sites: $Z > 2.58$, $p < 0.01$.

^eRural Taiwan villages versus U.S. sites: $Z > 2.58$, $p < 0.01$.

^fMetropolitan Taipei versus U.S. sites: $Z > 2.58$, $p < 0.01$.

The first methodological question is whether *DSM-III* diagnoses are appropriate for Taiwan. Certain authors suggest that *DSM-III* categories overlook several areas of psychopathology in Chinese cultures (16). Others question the use of "Western" psychiatric taxonomies, stating that psychiatric phenomena must be looked at in a culture-specific context (17). *DSM-III* criteria, therefore, are automatically rejected because they were not developed in the context of the culture being studied. These arguments can be challenged on several grounds. *DSM-III* has received widespread acceptance among psychiatrists throughout the world, and its diagnoses are felt to be appropriate and useful by those who have imported this taxonomy to their own cultures (18–20). Clinical experience by the Taiwanese authors of this paper supports the use of *DSM-III* diagnoses in Taiwan. A textbook written by Hwu (21) for use in Taiwan uses specific diagnostic criteria very similar to those of *DSM-III*. In addition, previous studies validate the use of *DSM-III* diagnoses in Taiwan (9, 14, 22, 23).

Second, the Taiwan Psychiatric Epidemiological Project and the ECA survey were designed and implemented somewhat differently, as noted earlier. However, despite these minor differences, both studies generated diagnoses standardized to their respective general population sampling frames. Results from each study can be compared because they represent prevalence rates from defined general population samples. Differences in results could be explained by different demographic structures of the sampling frames. This question has been looked at previously by standardizing the Taiwan sample to the U.S. sample, and differences were still found (15).

Third, the most common methodological problem in cross-cultural research (16), that of different diagnostic criteria and methods in the cultures being compared, was specifically addressed by the current study. The Taiwan Psychiatric Epidemiological Project and the ECA survey applied nearly identical diagnostic instruments to respondents from comparable community samples, and the data were analyzed with a single diagnostic algorithm. This solved the potential problem of different diagnostic criteria and methods.

Social or cultural differences may also have influenced our findings, and different hypotheses can be examined in light of the present study. One hypothesis is that the degree of urbanization may be associated with the rates of certain disorders. This may be a corollary to "degree of Westernization" in Taiwan because Taipei has been more influenced by Western technology and industry than the small towns or rural villages. One might expect a trend in which the rate of relevant disorders in the small towns is between those in Taipei and rural villages. This pattern was not found in any consistent way. Even for alcohol abuse/dependence, which might be expected to be most sensitive to Western influence, the most urbanized areas in Taiwan had only an intermediate rate. Therefore, degree of urbanization or Westernization provides little illumination of the differences in prevalence rates.

A second hypothetical explanation can be drawn from the observations that Taiwanese people are quite reluctant to discuss psychological information and that psychiatric disorder is severely stigmatized in Taiwan (16, 24, 25). For these reasons, people may be reluctant to endorse psychological symptoms and so would not

report them as symptoms on the DIS-CM. Furthermore, an emphasis on privacy in Taiwan may have compounded a response bias. In the ECA survey, respondents may be more expressive in their endorsement of symptoms because Americans are less likely to feel stigmatized by admitting to symptoms, are less concerned with privacy in an interview setting, and are less reticent about discussing personal information. This would lead to an apparently lower rate of illness in Taiwan even though the "true" rate of illness might be much closer. Such reluctance to endorse psychological and therefore stigmatizing symptoms could partially explain the generally lower rates of psychiatric disorder found in Taiwan. Evidence in support of this hypothesis should be discernible by comparing "highly stigmatizing" and "less stigmatizing" disorders.

The first disorder to consider in this regard is cognitive impairment. This condition represents a special case in that no symptoms are probed in the DIS, but rather a test, the Mini-Mental Status examination, is administered; therefore, a social stigma/cultural reticence effect, if any, is nullified. Although the national rate is possibly significantly lower in Taiwan, the rates at the individual sites in the United States and Taiwan are quite similar. This similarity of rates is consistent with the proposed hypothesis.

Also consistent with the social stigma/cultural reticence hypothesis is that rates of dysthymic disorder are more similar cross-nationally than are rates of major depression. Furthermore, the rate of major depression is higher than the rate of dysthymic disorder at all sites in the United States, while the rate of dysthymic disorder is higher than that of major depression at the Taiwan sites. If respondents in Taiwan tend to minimize their pathology, those with a history of major depression may meet criteria only for the less severe dysthymic disorder.

Generalized anxiety disorder, which consists of symptoms considered common in Taiwan (10, 24, 25), has virtually the same rate in Taiwan as in the United States. The symptom questions included in the criteria for generalized anxiety disorder focus on somatic symptoms such as motor tension, autonomic hyperactivity, and hypervigilance. Endorsement of these symptoms may be more acceptable to respondents in Taiwan (21, 24-26), and, therefore, rates may be less affected by a negative response bias.

Rates of alcohol and drug abuse and antisocial personality are each much lower in Taiwan. These diagnoses are derived from symptom criteria that are likely to be considered relatively more stigmatizing in Taiwan. Their lower rates may be attributed in part to a response bias. For schizophrenia, which has symptoms that are highly stigmatizing, some questions remain. The comparison of national rates shows a significantly lower rate in Taiwan, which is consistent with the social stigma/cultural reticence hypothesis. However, the comparison at individual sites is less robust. This may be because of the low base rate of the disorder.

On the other hand, the criteria for major depression

and panic disorder would not be considered so stigmatizing in Taiwan; yet, these disorders have lower rates in Taiwan. In addition, although some cases of dysthymic disorder in Taiwan may represent "true cases" of major depression, when dysthymic disorder and major depression are combined, the rates are lower in Taiwan. For obsessive-compulsive disorder and phobic disorder, the effects of social stigma and cultural reticence are unclear; yet, these disorders also have lower rates in Taiwan. For three diagnoses—manic disorder, schizophreniform disorder, and somatization disorder—the base rates were so low in both countries that comparisons are not meaningful. On the basis of this conflicting evidence and the personal experience of the Taiwan authors, cultural reticence and social stigma are felt to be an inadequate explanation for the lower rates of psychiatric illness in Taiwan.

One further possible explanation for the lower rates of illness in Taiwan is seen in an article by Hwu and associates (22). This article suggests that several diagnoses are seriously underestimated by the DIS-CM on the basis of the age distribution of cases. For several diagnoses, the expected increase in lifetime prevalence rate with increasing age was not found. The authors suggest that this trend indicates that the DIS-CM underestimates the lifetime prevalence rates of these disorders. Such underestimation might explain the lower rates in Taiwan. However, similar secular trends have been noted in the ECA survey (27). For many disorders, lower than expected rates of illness were found in the older cohorts of the ECA survey. Although a detailed and specific comparison of secular trends in the Taiwan Psychiatric Epidemiological Project and the ECA survey has not been performed, analyses to date show that secular trends are unlikely to explain the generally lower rates of psychiatric illness found in Taiwan.

CONCLUSIONS

Marked differences in the lifetime prevalence rates of most psychiatric illnesses were found between the United States and Taiwan. Because of the rigorous comparability of the methods used to study the populations, these differences are thought to be valid. While an understanding of cultural conditions in the United States and Taiwan informs our interpretation of these results, no single factor has yet been discerned that can explain the lower rates. Severe social stigma associated with mental illness, cultural reluctance to endorse symptoms, and the paramount importance of privacy may account for some of the differences in rates of illness but are unlikely to account for all of the differences. Similarly, a difference between the United States and Taiwan in secular trends of diagnostic prevalence rates is unlikely to explain the lower rates in Taiwan.

The current study demonstrates that it is feasible to apply modern epidemiological tools in widely disparate cultures and confirms the viability of combining DIS data from diverse sites. A detailed cross-cultural

comparison of symptom patterns is shown to be possible and will be pursued. Hypotheses concerning age at onset, symptom clustering, severity of symptoms, comorbidity, and chronicity of illness can now be explored in great detail. Just as our examination of specific diagnoses has improved our understanding of cross-national differences and similarities of psychiatric illness, so may a close inspection of specific symptoms and details of sociodemographic data complement our understanding. Having the data from the ECA survey and the Taiwan Psychiatric Epidemiological Project in a single data bank makes such comparisons possible.

As data from other international studies with the DIS become available, they might be added to the current data bank so that broader international comparisons could be performed. The current study can be viewed as a precursor of the upcoming Composite International Diagnostic Interview studies, which will be part of the next generation of cross-cultural surveys (28). Our efforts to use a rigorous methodology both in the collection of data from different cultures and in a standardized analysis of the data can serve as a model for these future research projects.

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Comorbid Association of Autism and Schizophrenia

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Objective: In the last several decades, considerable evidence has suggested that autism and schizophrenia are unrelated. However, recent reports have suggested that individuals with autism may be at greater risk for schizophrenia and that the conditions may be more closely related than generally believed. **Method:** The authors examined detailed case records of 163 adolescents and adults with well-documented histories of autism. These cases included 139 males and 24 females. **Results:** Only one individual had an unequivocal history of schizophrenia. **Conclusions:** If the present study group is taken to be representative, it appears that the frequency of schizophrenia among autistic patients (0.6%) is roughly comparable to the frequency of schizophrenia in the general population. It does not appear that the two conditions are more commonly observed together than would be expected on a chance basis; therefore, the current (DSM-III-R) approach to dual diagnosis of these conditions appears reasonable. (Am J Psychiatry 1991; 148:1705-1707)

Kanner (1) did not originally believe that autism and schizophrenia were related, but subsequent investigators (2) viewed infantile autism as the earliest manifestation of schizophrenia. This latter view was based, in large part, on an assumption of continuity of severity as well as broader views of schizophrenia (3). However, in the 1960s and 1970s various lines of evidence emerged suggesting that the two disorders were unrelated (4, 5); in addition, it appeared that schizophrenia of childhood onset was probably even less common than autism (6). In response to the increasing evidence of the validity of autism apart from schizophrenia, it was first included as an official category in *DSM-III* within a new class of disorder—pervasive developmental disorder. In recognition of the research suggesting that autism was not a form of schizophrenia, the *DSM-III* definition of autism specifically excluded individuals with hallucinations or delusions from receiving a diagnosis of autism.

Although many advantages of the *DSM-III* approach to the diagnosis of autism and the diagnosis of schizophrenia in childhood were apparent, certain as-

pects of the definitions proved problematic (7, 8). For example, it was unclear why having autism would necessarily act to protect an individual from subsequently developing schizophrenia (9). Petty et al. (10) reported three cases of autism associated with schizophrenia and argued that this association was unlikely to occur by chance alone. In *DSM-III-R*, autism and schizophrenia were no longer mutually exclusive diagnostic categories, although criteria for schizophrenia indicated that this additional diagnosis was warranted only if an individual with autism exhibited prominent delusions and/or hallucinations. As noted by Petty et al. (10), a greater than expected association of the two conditions would have implications both for syndrome definitions (in *DSM-IV*, for example) and for research and would call into question the view that the disorders are unrelated (4).

METHOD

Detailed case records of 163 adolescents and adults with well-documented histories of autism were examined as part of this study. The cases of these patients, 139 males and 24 females, were selected for review from among a series of consecutive patients evaluated at our center over the past decade. All patients had previously received a diagnosis of autism according to Rutter's criteria (11). Given the apparent rarity of strictly diagnosed schizophrenia in preadolescent children (12), patients were included in the review only if the individual was at least 15 years of age at the time of most recent follow-up (i.e., school-aged children and very young adolescents were excluded from the review).

The patients had received comprehensive evaluations

Received Oct. 4, 1990; revision received May 16, 1991; accepted June 14, 1991. From the Child Study Center, Yale University. Address reprint requests to Dr. Volkmar, Child Study Center, Yale University, P.O. Box 3333, New Haven, CT 06510.

Supported by a grant from the McArthur Foundation to APA and by grants HD-03008 from the National Institute of Child Health and Human Development and MH-14696 from NIMH.

The views expressed in this article are those of the authors and do not represent the official positions of APA or its DSM-IV Task Force or Work Groups.

The authors gratefully acknowledge John Werry's helpful comments.

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(including psychiatric examination, psychological testing, and speech/communication examinations) and were followed periodically at our center, typically on at least an annual or biennial basis. Patients were known personally to one or both of the raters (F.R.V. and D.J.C.). In addition to materials derived from examinations performed at our center, other records, typically including medical records and extensive educational reports, were available.

The mean \pm SD age of the patients at review was 24.1 \pm 5.58 years (range=15–41). As expected, most individuals less than 21 years old lived with their parents and received a number of special educational services. Adult patients were in various residential placements, most commonly in group homes, although some continued to live with parents and a few lived independently. Full-scale IQ scores, based on results of various standard tests, were available for 151 patients. Seventy-eight (47.9%) of the patients were largely or entirely mute (e.g., they said no words or only echoed language). As expected, female patients were, on average, more severely affected; for example, they were significantly more likely to be mute ($\chi^2=3.99$, $df=1$, $p<0.05$) and had lower IQs ($t=2.63$, $df=149$, $p<0.01$) than the male patients. The characteristics of the group are consistent with those of other consecutive case series (13).

Case records were reviewed by one or both raters using a two-stage procedure. At the initial review cases were flagged for subsequent, more detailed examination if the individual had been noted by professionals, teachers, or parents ever to have exhibited any two of the following symptoms suggestive of schizophrenia: delusions, hallucinations, incoherence, loosening of associations, catatonic behavior, unusual sensory experiences typical of schizophrenia, and markedly peculiar behaviors other than the stereotyped, self-stimulatory behaviors and restricted range of interests typical of autism. In addition, the records of any patient who had been hospitalized psychiatrically were selected for more detailed review. The intent of the initial screening procedure was to identify patients with at least some likelihood of exhibiting schizophrenia.

On the basis of the initial review, the records of 41 patients (33 males and eight females) were examined in greater detail by the raters, who independently applied *DSM-III-R* criteria for a lifetime (i.e., present or past) diagnosis of schizophrenia. As might be expected, given the importance of verbal abilities in the definition of schizophrenia and the marked communication problems associated with autism, these 41 patients were all capable of truly communicative speech and exhibited higher intellectual levels than the rest of the study group (mean IQ=57.6 \pm 26.2 versus 39.5 \pm 24.6, respectively, $t=3.96$, $df=149$, $p<0.001$). Levels of absolute agreement between the raters on individual *DSM-III-R* schizophrenia criteria were quite high; however, the low base rate of positive criteria limited the value of usual, chance-corrected reliability indexes.

RESULTS

A *DSM-III-R* diagnosis of schizophrenia was made unequivocally and independently by both raters in one case. In one other case a patient had received a diagnosis of schizophrenia at the time of psychiatric hospitalization but this diagnosis was not made at discharge from the hospital and the individual was not felt by either of the two raters to have clearly fulfilled *DSM-III-R* criteria at any point.

The one patient who was given comorbid diagnoses of autism and schizophrenia had been followed for many years at our center after his diagnosis of autism was made in early childhood. He had consistently functioned in the mildly mentally retarded range and had always attended special schools. Around age 15 his behavior began to change. He became more preoccupied, started to talk aloud, and complained of auditory and occasional visual hallucinations. Auditory hallucinations included voices that commented on his behavior and urged him to use magical powers. His speech became difficult to follow, and he exhibited catatonia on at least one occasion. Schizophrenic symptoms gradually increased in severity and intensity and he was hospitalized. The diagnoses of autistic disorder and schizophrenia were made during the hospitalization at both the time of admission and the time of discharge. He was treated with various neuroleptic medications with partial remission of the hallucinations. He continues to exhibit some residual symptoms of schizophrenia. There was a strong family history of schizophrenia.

In the second case a high-functioning, nonretarded autistic man had been hospitalized briefly after an episode of disorganized behavior. The admission diagnosis of schizophrenia was made in view of his disorganization, obvious premorbid oddity, and what appeared to be delusions. This man had previously achieved a considerable degree of personal independence; the hospitalization was precipitated by a change in his living arrangements and his difficulty tolerating the attendant changes in his routines. Despite the initial impression of schizophrenia at admission the patient never exhibited hallucinations. The initial impression of delusions appeared to reflect longstanding patterns of unusual interests and preoccupations. At discharge a diagnosis of autistic disorder rather than schizophrenia was made. At follow-up the patient continued to exhibit marked social isolation, resistance to change, unusual communication patterns, and unusual interests but had returned to his previous level of functioning.

The 39 other individuals included in the second level of case examination were noted to exhibit at some time at least some symptom or symptoms that might be taken as "suggestive" of schizophrenia, e.g., unusual sensory experiences, difficulties in distinguishing fantasy and reality, or bizarre preoccupations and interests. However, true delusions and/or hallucinations were not unequivocally present in these patients and, as far as could be determined, the patients did not meet *DSM-III-R* criteria for schizophrenia at any point. For

example, one high-functioning man reported unusual sensory experiences that were not associated with specific content. Similarly, instances of unusual interests and preoccupations revolved around the highly circumscribed or idiosyncratic interests sometimes observed in high-functioning individuals with autism (e.g., one young woman was preoccupied with Cambodia), but such instances did not clearly involve ideas of reference or control, thought broadcasting, etc. As expected, individuals who were largely or entirely mute could not be said to exhibit any symptoms suggestive of delusions or hallucinations.

DISCUSSION

The limitations of the present study must be noted. The data were derived from chart review using a consecutive case series rather than an epidemiologically based sample. In addition, it is possible, of course, that schizophrenia may develop in additional patients as they are followed over time. It is theoretically possible that an individual might have exhibited a schizophrenic disorder for a brief period that was of such short duration and/or of such minimal severity as not to have been noted. This latter seems unlikely, however, because the patients were personally known and often well-known to the raters and detailed information was available about each patient from different sources. Most of the patients had also been followed on a regular basis. The size of the study group also lends interest to the results.

In this study only one individual unequivocally exhibited schizophrenia; a diagnosis of schizophrenia had been made by other clinicians in a second patient but appeared highly questionable. If the present study group is taken to be representative, it appears that the frequency of schizophrenia (0.6%) is roughly comparable to the frequency of schizophrenia in the general population (14).

The earlier case reports of an association between the two disorders (10) did not provide information on the frequency of schizophrenia in a larger study group of autistic individuals. Other case reports of adult psychotic illness superimposed on autism or related conditions have also appeared (15), but it is not surprising that at least a few persons with autism also develop schizophrenia, given the frequency of schizophrenia in the general population and the presumption that having autism does not act to *protect* an individual from subsequent schizophrenia. Some point of general phenomenological similarity is also suggested by Kanner's use of the term "autism" (1).

It is, of course, difficult to make a diagnosis of schizophrenia in subjects who are largely or entirely mute (usually about 50% of autistic samples). To some extent these parallel the difficulties observed in making a diagnosis of schizophrenia in young (preschool and school-aged) children, where it is clear that adult concepts of reality have not fully emerged and magical thinking and beliefs in fan-

tasy figures are common (3). Among high-functioning autistic adults, peculiar interests, preoccupations, and experiences may similarly pose problems in differential diagnosis. Clearly, such unusual features, although typical of autism, may pose potential sources of confusion for clinicians who have less experience with autistic individuals. However, in the patients in this case series it was generally quite clear that these features were of long standing, were generally highly circumscribed, and were a source of some gratification. Except in the one instance where the additional diagnosis of schizophrenia appeared very clearly to be justified, these features did not seem to be associated with deterioration in levels of previously achieved functioning.

Although the study of individuals who exhibit both autism and schizophrenia may be of interest for other reasons, it does not appear that the two conditions are more commonly observed together than would be expected on a chance basis. The current (*DSM-III-R*) approach to dual diagnosis of these conditions appears reasonable.

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Cocaine-Induced Paranoia and Psychosis Proneness

Sally L. Satel, M.D., and William S. Edell, Ph.D.

Objective: The aim of this study was to determine whether individuals who experience transient cocaine-induced paranoia are vulnerable to psychosis. **Method:** The subjects were 20 cocaine-dependent men who had been using more than 5 g of cocaine per week and were undergoing substance abuse treatment; half reported binge-limited cocaine-induced paranoia. The men were assessed with the Perceptual Aberration Scale and the Magical Ideation Scale, self-report measures of symptoms thought to precede the development of functional psychosis. **Results:** The combined scores on the Perceptual Aberration Scale and Magical Ideation Scale were strongly correlated with a history of cocaine-induced paranoia. The sensitivity, specificity, and positive and negative predictive power were 80.0%, 90.0%, 88.9%, and 81.8%, respectively. **Conclusions:** Heavy cocaine users who experience transient paranoia while intoxicated may be at higher risk for development of psychosis than cocaine users who do not experience paranoia.

(Am J Psychiatry 1991; 148:1708-1711)

It is well known that drugs of abuse can produce both transient and persistent psychotic symptoms in individuals without histories of primary psychotic illness (1-3). Whether such individuals possess an underlying predisposition to psychosis in the absence of pharmacologic stress is unknown. Evidence of such a predisposition has been provided by several studies.

Tsuang et al. (4) studied consecutively admitted substance users with and without psychosis. Use of hallucinogens and cannabinoids was highly prevalent in the 72 substance abusers who developed psychoses; their premorbid histories and symptoms were comparable to those of a group of schizophrenic patients. By contrast, a comparison group of 30 substance abusers who did not develop psychosis tended to use drugs without psychotomimetic properties—barbiturates, benzodiazepines, and opiates. Bowers and Swigar (5) examined 95 patients hospitalized for acute psychosis; 60 had used hallucinogens within 3 years of admission. Among the male subjects, those with positive family histories of major mental illness appeared capable of becoming psychotic with relatively small amounts of hallucinogen, whereas those without such histories required greater exposure. In a 6-year follow-up of 11 amphetamine users who were asymptomatic at the time of initial treatment, McLellan et al. (6) diagnosed seven as psychotic; none of the opiate abusers or alcoholics was psychotic

at follow-up. These investigators and others (1, 7, 8) have speculated that subthreshold psychotic symptoms may have actually influenced the subjects' selection of drugs and that symptoms associated with psychotic disorders may have been present but below the limit of clinical detection at the time drug use began.

Cocaine use has been associated with paranoia, but not all users develop this symptom despite prolonged and heavy exposure (9-11). In our earlier study (12) of 50 cocaine-dependent men, none of whom had other axis I diagnoses, 34 (68%) reported paranoid episodes limited to their periods of cocaine use. The paranoia did not extend beyond the "crash," or hypersomnolent phase, of early cocaine abstinence. The paranoia had developed after an average of 3 years' use. Importantly, the subjects reporting paranoia did not differ significantly from those not reporting paranoia with respect to use characteristics such as route of administration, lifetime duration of use, cumulative exposure to cocaine, amount of cocaine consumed in month of admission, or concurrent use of other drugs. These findings suggest that development of paranoia is not simply the result of exceeding a threshold of use and that affected individuals may be predisposed to this drug-induced state.

Chapman et al. have developed a series of objective scales that attempt to identify individuals at higher than normal risk for psychosis. Two of the most promising scales measure perceptual aberrations (13) and magical ideation (14). These scales ascertain, through self-report, experiences that are characteristic of nascent psychotic states. Numerous published studies (15-20) have documented the reliability and validity of these instruments. Unlike the standard approach of studying the

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relatives of psychotic patients, which may generate an unrepresentative and restricted risk sample, this strategy measures symptoms that are thought to precede psychosis and allows for the study of a greater variety of individuals with psychotic diathesis (16).

In the present study we attempted to answer the question of whether individuals who display transient cocaine-induced paranoid symptoms are predisposed to psychosis. We hypothesized that scores on the scales of psychosis proneness would discriminate between individuals who display such paranoid symptoms and those who do not.

METHOD

Subjects

The subjects were recruited from patients consecutively admitted to the inpatient and outpatient units of a VA substance abuse treatment program. A total of 32 patients were screened with the Cocaine Experience Questionnaire (description to follow). The first 10 patients who reported binge-limited (transient) paranoid experiences during cocaine intoxication and the first 10 who denied such experiences were included. It was necessary to exclude 12 patients to achieve this distribution because patients who reported paranoia were overrepresented among the heavy cocaine users (12, 21). The subjects were assigned to groups blindly, i.e., the subjects were determined to be psychosis prone by one author (W.S.E.), who had no knowledge of the specific subjective response to cocaine, and the response to cocaine was determined by the other author (S.L.S.). The inclusion criteria for the study were as follows.

1. Primary *DSM-III-R* axis I diagnosis of cocaine dependence and a minimum of 3 years of continuous use of at least approximately 5 g of cocaine per week. The latter requirement was based on our earlier work (12), which demonstrated that development of paranoia in vulnerable individuals occurs after an average of 3 years' use of at least 5 g of cocaine per week.

2. No concurrent *DSM-III-R* substance dependence diagnosis or other axis I affective or psychotic disorder. A patient who used another substance was included if the substance was used to modify the acute effects of cocaine and if such use did not take place in the absence of cocaine intoxication.

3. No prior psychiatric hospitalizations except for detoxification and rehabilitation.

4. Absence of psychotic symptoms or paranoia outside the context of cocaine use.

5. Absence of *DSM-III-R* axis II diagnoses of schizotypal or schizoid personality disorder.

6. Negative family history of psychosis in first-degree relatives.

The study was designed so that the final group of 20 male subjects was equally divided between those reporting cocaine-induced paranoia and those not reporting such symptoms. All those invited agreed to participate.

Instruments

The Cocaine Experience Questionnaire contains 58 items and assesses methods and patterns of cocaine use and the extent and nature of the paranoid experiences associated with use. Family history of functional psychotic symptoms was elicited during administration of the questionnaire. The subjects were carefully instructed to distinguish adaptive hypervigilance or anxiety in high-risk situations (e.g., making drug deals, passing through housing projects, engaging in illicit activities) from completely irrational beliefs (e.g., the perception that the police were standing on the window ledge outside the subject's 10th-floor apartment). This questionnaire was administered by a rater and typically took 20 minutes for a subject who did not report paranoid experiences and 30–45 minutes for a subject who did.

The original development of the Scales of Psychosis Proneness largely followed the sequential steps recommended by Jackson for development of personality scales (22). Items were written and judged according to how well they met trait specifications based on Meehl's descriptions (23) of these characteristics. Careful attention was given to minimizing bias due to social desirability and acquiescent response style while maximizing item-scale correlations.

The Perceptual Aberration Scale is a 35-item true-false measure of perceptual distortions of body image and of visual and auditory stimuli (13). Analyses of internal consistency (13) have revealed alpha values around 0.90 and negligible correlations with age, education, social class, social desirability, and acquiescent response style. Stability of scores, as shown by test-retest reliability coefficients, is high ($r=0.75$) (17). Representative items (and answers indicating perceptual distortion) include "Parts of my body occasionally seem dead or unreal" (true) and "My hands or feet have never seemed far away" (false).

The Magical Ideation Scale is a 30-item true-false scale that measures belief in forms of causation that by conventional standards are invalid (14). Negligible correlations with age, education, social class, social desirability, and acquiescent response style have been observed (14). Internal consistency has been shown by coefficient alphas in the mid 0.80s, and stability of scores is indicated by test-retest reliability coefficients of 0.80 (17). Representative items (and answers indicating magical ideation) include "Some people can make me aware of them just by thinking of me" (true) and "Horoscopes are right too often for it to be a coincidence" (true).

The subjects were given special instructions for filling out the Perceptual Aberration Scale and Magical Ideation Scale. They were told that an occasional item might refer to an experience they had had only when taking drugs and that, unless they had had the experience at other times, they were to mark the item as if they had *not* had that experience.

The mean \pm SD score on the Perceptual Aberration Scale was 6.85 ± 7.16 , whereas the median was 5.00, in

dicating the distribution of scores was positively skewed. The mean score on the Magical Ideation Scale was 10.15 ± 6.12 , and the median was 8.50, so the distribution of scores on this scale was also positively skewed. These group scores were virtually identical to scores on these instruments for large samples of male undergraduate students (Perceptual Aberration Scale = 6.87 ± 6.06 ; Magical Ideation Scale = 9.73 ± 5.83) (L.J. Chapman and J.P. Chapman, unpublished norms, April 11, 1989), which showed similarly skewed distributions. As noted by Lenzenweger and Loranger (20), however, there are no established cutoff scores for use in classifying individuals among nonstudent clinical populations as at high and low risk for psychosis. Given the skewed distribution of scores in our group, we followed their strategy of dividing subjects at the group median, which we defined as the total of the median scores on the Perceptual Aberration Scale and Magical Ideation Scale, 13.5. Thus, subjects who scored 13 or lower were considered low risk and those who scored above 13 were designated high risk.

RESULTS

Of the 10 subjects who reported cocaine-induced paranoia, eight scored above the combined median score on the Perceptual Aberration Scale and Magical Ideation Scale. Of the 10 who did not report cocaine-related paranoia, only one scored above the median. The strong positive correlation between cocaine-induced paranoia and psychosis proneness (Fisher's exact test, $p=0.003$; phi coefficient = 0.7035, $p<0.005$) represents a very large effect size (24), accounting for almost 50% of the shared variance. It should be noted that in this group the base rate, or proportion of individuals who developed cocaine-induced paranoia, was 50.0% (10 of 20) and the selection ratio, or proportion of individuals who were predicted to be psychosis prone, was 45.0% (nine of 20), so the maximum possible phi coefficient was 0.9045. Only if the base rate and selection ratio are equal can a test achieve perfect validity (i.e., $\phi=1.00$) (25). The sensitivity, or probability of the symptom of paranoia given the diagnosis of psychosis proneness, was 80.0%. The specificity, or probability of not having cocaine-induced paranoia given the absence of psychosis proneness, was 90.0%. The positive predictive power, or probability of psychosis proneness given the presence of paranoia, was 88.9%. The negative predictive power, or probability of not being psychosis prone given the absence of paranoia, was 81.8%.

DISCUSSION

The present study provides evidence that individuals who experience transient cocaine-induced paranoia report symptoms, occurring in the drug-free state, that are associated with psychosis proneness. As the study was cross-sectional and correlational, it is impossible to determine direction of causality. That is, does the experience of cocaine-induced paranoia (or, perhaps, the

drug-induced neurobiologic changes underlying this symptom) increase the likelihood of having perceptual aberrations and magical ideation, or are these latter experiences an expression of an intrinsic vulnerability to paranoia that predated cocaine consumption in otherwise asymptomatic individuals?

Chronic cocaine use affects dopaminergic systems (26, 27). These systems have long been associated with schizophrenia. Thus, cocaine self-administration may represent a quasinaturalistic method for stressing the neurotransmitter system most often linked to the positive symptoms of schizophrenia.

Some individuals respond to the pharmacologic stress of cocaine by developing transient paranoid symptoms, and it is largely these individuals whose scores on the two scales of psychosis proneness were in the high-risk range. Perhaps those who develop transient cocaine-induced paranoia possess intrinsic, subclinical vulnerability of the dopaminergic system, a marker of which is endorsement of specific responses on these scales. Although speculative, the concept that dopaminergic dysregulation may underlie forms of both functional and drug-induced paranoia is of considerable heuristic value in the investigation of neurobiological mechanisms of vulnerability to psychosis.

It seems reasonable to hypothesize that such individuals are at high risk for development of prolonged psychosis, particularly of paranoid quality, when under pharmacologic or emotional stress. Indeed, the intensity of paranoia and the rapidity of its onset during cocaine binges appear to increase over time, consistent with sensitization (12, 21). Brady et al. (28) reported that schizophrenic patients who abused cocaine were significantly more likely to be of the paranoid subtype than were schizophrenic patients who did not use cocaine. The relationship between the pharmacologic stress of chronic cocaine exposure, the development of paranoid symptoms, and the onset of psychosis is unknown. Clearly, larger-scale studies with a longitudinal prospective design are required for full exploration of this question and for definitive determination of whether deviant responses on the proneness scales precede the development of cocaine-induced paranoia in persons just beginning long-term cocaine abuse.

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Clinical Phenomenology and Neurobiology of Cocaine Abstinence: A Prospective Inpatient Study

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Objective: This study was undertaken to document symptoms and changes in dopaminergic function emerging after abrupt cessation of cocaine use. **Method:** After admission, 22 patients with DSM-III-R cocaine dependence were observed drug free for 3 weeks. The patient-rated Ribicoff Abstinence Rating Scale, Symptom Rating Scale, Physical Symptom Scale, Patient Rated Anxiety Scale, Beck Depression Inventory, and visual analogue scales for 16 subjective states were completed daily, and nurses rated 13 patients with the global anxiety and depression items of the Short Clinical Rating Scale. Serial blood samples were obtained three times weekly, and the patients' levels of prolactin, growth hormone (GH), and homovanillic acid (HVA) were measured. Their prolactin and GH values were compared with those of matched normal subjects. **Results:** A total of 62 subjective symptom variables were evaluated. At baseline, the symptom ratings were mildly elevated. At 3 weeks there were significant decreases from baseline in 28 variables and nearly significant decreases in six additional variables. Nurse-rated anxiety and depression also changed, but in a more variable pattern. There was a small but significant increase from baseline over time in plasma prolactin, but there were no significant changes in GH or HVA. The patients' prolactin and GH values did not differ from those of the normal subjects. **Conclusions:** These findings suggest that symptoms after inpatient cessation of uncomplicated cocaine addiction are relatively mild and decrease linearly over the first month. Evidence of dysregulated central dopamine function was limited. The findings do not support routine use of pharmacological agents in the inpatient management of such patients.

(Am J Psychiatry 1991; 148:1712-1716)

A critical question involving cocaine abuse is whether prolonged ingestion leads to clinically significant withdrawal upon abrupt discontinuation. Until the early 1980s, most authorities (1, DSM-III) discounted this possibility and, consequently, the possibility of true physiological dependence. More recently, however, it has been argued (2, 3) that heavy users manifest a characteristic syndrome upon abrupt cessa-

tion of cocaine use. The issue has been obscured by the nature of severe, chronic cocaine use: unlike alcohol and opiate dependence, which involve daily ingestion, severe cocaine use is characterized by prolonged, high-intensity binges alternating with periods of relative abstinence (4). The occurrence of dysphoric and neurovegetative symptoms during the hours after such a binge (the "crash") is widely accepted by users and clinicians (5), but whether these or subsequent symptoms represent withdrawal, and therefore physiological dependence, is still debated.

Documentation of cocaine withdrawal phenomena has been limited. Subjective reports from detoxifying cocaine users describe fatigue, depressed mood, agitation, diaphoresis, nausea, sleep disturbance, paranoia, and drug craving (6, 7). Attempting to organize these observations, Gawin and Kleber (5) advanced a triphasic model of postbinge symptoms. They hypothesized that an initial and severe "crash" (phase 1: 9 hours to 4 days) is followed by a protracted period of milder

Received Feb. 12, 1991; revision received May 22, 1991; accepted June 14, 1991. From the Clinical Neuroscience Research Unit, Abraham Ribicoff Research Facilities, Connecticut Mental Health Center; the Psychiatry Service, West Haven VA Medical Center, West Haven, Conn.; and the Department of Psychiatry, Yale University School of Medicine, New Haven, Conn. Address reprint requests to Dr. Price, Connecticut Mental Health Center, 34 Park St., New Haven, CT 06519.

Supported in part by grant DA-04060 from the National Institute on Drug Abuse, by grants MH-25642 and MH-36229 from NIMH, and by the Department of Mental Health, State of Connecticut.

The authors thank Huan Gao, M.S., Deborah Herbst, M.S., and Sally Trufan for help with the data analysis.

"withdrawal" (phase 2: 1 to 10 weeks), succeeded finally by an indefinite period of "extinction" (phase 3), characterized by no symptoms and episodic craving. These changes were believed to reflect disturbances in central dopamine function secondary to long-term cocaine use.

In the only independent test of this model, Weddington et al. (8) recently assessed changes in mood, cocaine craving, and sleep during abstinence in a controlled study of 12 male inpatients. They found that dysphoria and craving decreased linearly during the 28-day study, and the most prominent changes occurred within the first few days of admission. Noting the absence of a "classic withdrawal pattern," they suggested that "short-term abstinence" more accurately described the phenomena they observed. Although Weddington et al. did not assess measures of dopamine function, other investigators have reported such measures to be higher than normal (9–13), lower than normal (13), and normal (14, 15) during abstinence from cocaine.

We undertook the present study to 1) prospectively document symptoms emerging during the first 3 weeks after abrupt cessation of cocaine use, 2) assess neurobiological measures reflecting dopamine function during this period, 3) determine whether the clinical and neurobiological findings are related, and 4) consider these findings in light of proposed models of cocaine withdrawal (5, 8). The neurobiological measures we assessed were plasma levels of prolactin (which is tonically inhibited by dopamine), human growth hormone (GH) (which is phasically stimulated by dopamine), and homovanillic acid (HVA) (a principal dopamine metabolite).

METHOD

Subjects

The subjects were 22 consecutive inpatients, 19 men and three women; 12 were black and 10 were white, and their mean \pm SD age was 33.8 \pm 7.5 years. They all gave voluntary informed consent to participate in the study. Thirteen were from a neuropsychiatric research facility, and nine were from a substance abuse treatment unit of a VA medical center. Direct examination by a psychiatrist (S.L.S., L.H.P., J.M.P.) determined that all patients met the *DSM-III-R* criteria for cocaine dependence. Any patient concurrently dependent on another substance or meeting criteria for another axis I disorder was excluded. All patients were determined to be free of serious medical illness. On admission, all patients claimed to have used cocaine within the preceding 24 hours and had urine samples that were positive for cocaine only. Patient referrals came from local emergency rooms, outpatient programs, and word of mouth. All of the patients had used cocaine almost continuously during the 6 months before admission. The amount used weekly was 12.3 \pm 9.0 g and the total duration of use was 5.3 \pm 4.7 years, so the estimated life-

time consumption was 2.85 \pm 2.71 kg. The cocaine was ingested by free-base smoking (N=17), intranasally (N=7), and intravenously (N=3).

The comparison group consisted of age- and sex-matched healthy subjects who were participating in related studies; 19 were male and three were female, and their age was 33.8 \pm 7.8 years. A psychiatrist (J.M.P., C.J.M., J.H.K.) using a semistructured interview established that the comparison subjects were free of personal and family histories of mental disorder. Any subject who had used psychoactive drugs within 4 weeks or alcohol within 2 weeks of testing was excluded.

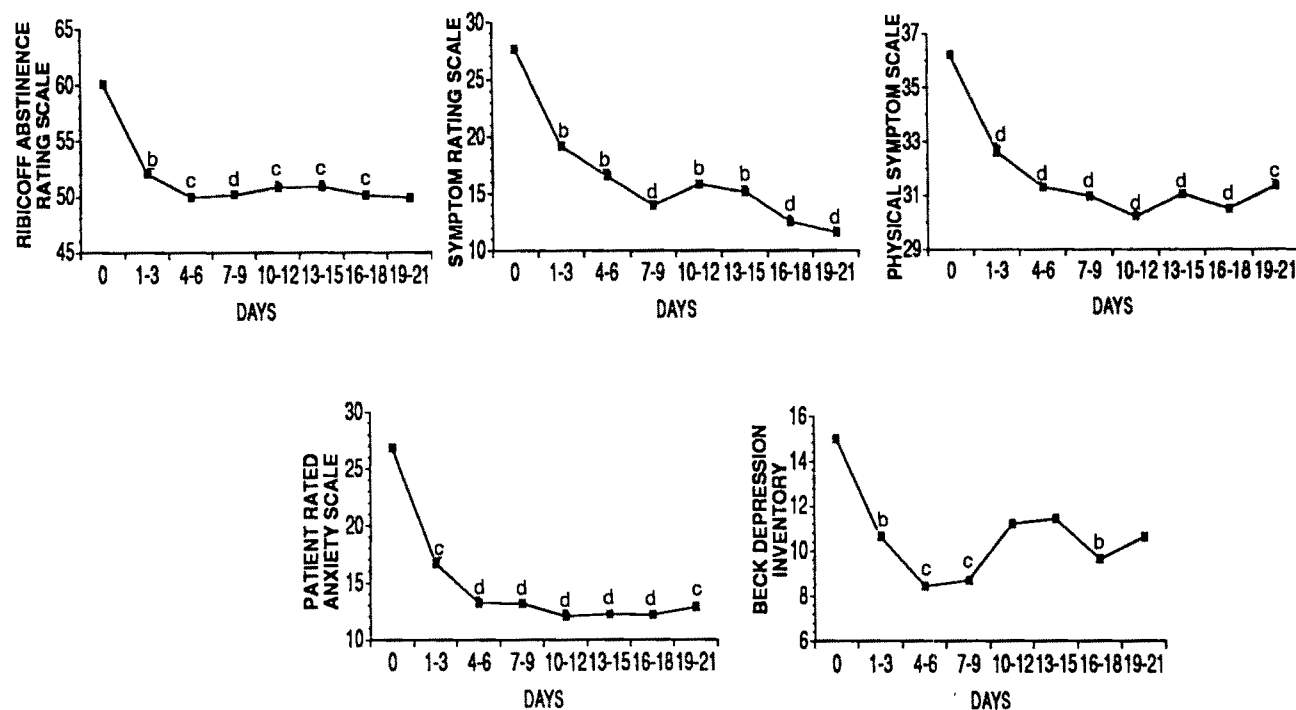
Procedures

After admission, the patients were restricted to their wards throughout the 21-day study, and they received no psychotropic drugs. Visitors were limited, and all visits were supervised. Supervised urine samples were randomly obtained from the patients approximately three times weekly; no positive urine samples were detected during the study.

On admission, the patients were assessed with the Cocaine Screening Test, the Quantitative Cocaine Inventory, and the Quantitative Cocaine History, self-report instruments that document the extent and consequences of drug use (4, 5). Starting on the day of admission, the patients received an extensive battery of somatic, behavioral, and psychological symptom ratings once or twice daily. The battery included the Ribicoff Abstinence Rating Scale (16), the Symptom Rating Scale (17), the Physical Symptom Scale (18), the Patient Rated Anxiety Scale (D.V. Sheehan, unpublished), the Beck Depression Inventory (19) (research unit patients only), and visual analogue scales (20) for 16 different subjective states (talkative, happy, drowsy, nervous, sad, calm, depressed, anxious, energetic, fearful, mellow, high, angry, irritable, craving for cocaine, and degree of discomfort relative to previous periods of abrupt abstinence from cocaine). Research nurses supervised completion of these instruments. The patients on the research unit were also rated twice daily by nurses using the global anxiety and depression items of the Short Clinical Rating Scale (21), which measures objective patient behavior over an 8-hour nursing shift.

Blood was obtained for assay of prolactin, GH, and HVA. Baseline postfast samples were drawn at 8:30 a.m., 18–22 hours after admission, and serial samples were drawn at this time every 2–3 days. Two postfast samples 15 minutes apart were also drawn from the healthy subjects at this time and assayed for prolactin and GH; HVA values were unavailable for the normal subjects. The normal subjects' prolactin and GH values were averaged to yield a single value for each measure.

Plasma was assayed for prolactin with a radioimmunoassay kit (Clinical Assays); the intra- and interassay coefficients of variation were 6% and 11%, respectively. GH was assayed with a homologous double-antibody method (National Institute of Arthritis, Metabo-

FIGURE 1. Mean Symptom Scores of 22 Cocaine-Dependent Patients During Initial 3 Weeks of Abstinence^a

^aThe ranges of possible scores were as follows: Ribicoff Abstinence Rating Scale, 41–205; Symptom Rating Scale, 0–72; Physical Symptom Scale, 27–108; Patient Rated Anxiety Scale, 0–144; Beck Depression Inventory, 0–63. The p values are based on paired t tests, time point versus baseline; see text for results of ANOVAs.

^bp<0.05.

^cp<0.005.

^dp<0.001.

lism and Digestive Diseases), and the intra- and inter-assay coefficients of variation were 5% and 7%. Plasma free HVA was measured by gas chromatography/mass spectroscopy with deuterated internal standards; all samples were run in duplicate (22).

The symptom ratings obtained on the day of admission and the biochemical measures taken within 18–22 hours of admission constituted the baseline values. The subsequent measures were averaged across 3-day periods to yield seven serial mean values for each variable. Change from baseline was evaluated with analysis of variance (ANOVA), followed by paired t tests when appropriate. For the biochemical measures, the normal subjects' values were compared by t test with the patients' values at baseline and at all subsequent intervals. The significance tests were two-tailed.

RESULTS

Symptom Ratings

Scores on 62 subjective symptom variables were evaluated: the 16 visual analogue scale ratings, the scores on the 41 individual items of the Ribicoff Abstinence Rating Scale, and the total scores on the Ribicoff scale, Symptom Rating Scale, Physical Symptom Scale, Patient Rated Anxiety Scale, and Beck Depression In-

ventory. At baseline, the patients' scores on these instruments were mildly elevated.

As shown in figure 1, over the 3 weeks of the study there were significant decreases in total scores on the Ribicoff Abstinence Rating Scale ($F=10.02$, $df=7, 126$, $p<0.0001$), Symptom Rating Scale ($F=6.91$, $df=7, 126$, $p<0.0001$), Physical Symptom Scale ($F=8.54$, $df=7, 126$, $p<0.0001$), Patient Rated Anxiety Scale ($F=8.02$, $df=7, 119$, $p<0.0001$), and Beck Depression Inventory ($F=2.33$, $df=7, 70$, $p<0.04$).

Of the 16 visual analogue scale ratings, there were significant decreases from baseline in the mean scores of four—abstinence discomfort ($F=6.42$, $df=7, 119$, $p<0.0001$), anxious ($F=5.14$, $df=7, 126$, $p<0.0001$), calm ($F=2.25$, $df=7, 112$, $p<0.04$), and drowsy ($F=2.21$, $df=7, 126$, $p<0.04$)—and there were nearly significant decreases in four—irritable ($F=2.04$, $df=7, 126$, $p<0.06$), mellow ($F=1.94$, $df=7, 119$, $p<0.07$), high ($F=1.91$, $df=7, 119$, $p<0.08$), and craving ($F=1.83$, $df=7, 126$, $p<0.09$).

Of the 41 individual items on the Ribicoff scale, there were significant decreases from baseline in 19—hypokinesia ($F=5.01$, $df=7, 126$, $p<0.0001$), hyperosmia ($F=4.75$, $df=7, 126$, $p<0.0001$), impaired concentration ($F=4.40$, $df=7, 126$, $p<0.0002$), hyperacusis ($F=4.27$, $df=7, 126$, $p<0.0003$), insomnia ($F=3.88$, $df=7, 126$, $p<0.0008$), muscle twitching ($F=3.70$, $df=7, 119$, $p<0.002$), hypoalgesia ($F=3.67$, $df=7, 119$,

$p < 0.002$), craving ($F = 3.48$, $df = 7, 126$, $p < 0.002$), hyperesthesia ($F = 3.40$, $df = 7, 126$, $p < 0.003$), rhinorrhea ($F = 3.34$, $df = 7, 126$, $p < 0.003$), photophobia ($F = 3.25$, $df = 7, 126$, $p < 0.004$), strange smells ($F = 2.99$, $df = 7, 119$, $p < 0.007$), myalgias ($F = 2.91$, $df = 7, 126$, $p < 0.008$), hypesthesia ($F = 2.81$, $df = 7, 119$, $p < 0.01$), decreased energy ($F = 2.68$, $df = 7, 126$, $p < 0.02$), piloerection ($F = 2.58$, $df = 7, 126$, $p < 0.02$), diarrhea ($F = 2.49$, $df = 7, 126$, $p < 0.02$), hyposmia ($F = 2.27$, $df = 7, 119$, $p < 0.04$), and optical distortions ($F = 2.25$, $df = 7, 119$, $p < 0.04$). There were nearly significant decreases in two—agitation ($F = 1.94$, $df = 7, 126$, $p < 0.07$) and strange tastes ($F = 1.87$, $df = 7, 126$, $p < 0.09$). Most other symptom variables also showed nonsignificant decreases from baseline over time.

The nurses' ratings on the Short Clinical Rating Scale showed significant changes in depression and anxiety, but the patterns of change were unlike those on the patient-rated measures: the depression ratings showed a progressive increase ($F = 3.16$, $df = 7, 70$, $p < 0.006$), and the anxiety ratings showed an initial decrease followed by a slight increase ($F = 2.63$, $df = 7, 70$, $p < 0.02$).

Biochemical Variables

The patients' mean plasma prolactin level increased slightly but significantly, from 10.4 ± 4.5 ng/ml at baseline to a maximum of 14.0 ± 4.5 ng/ml at days 19–21 ($F = 2.49$, $df = 7, 133$, $p < 0.02$). GH and HVA did not change significantly from baseline.

The normal subjects' prolactin and GH values did not differ significantly from the patients' values at baseline or at subsequent times.

DISCUSSION

These cocaine-dependent inpatients reported mild somatic, behavioral, and psychological symptoms on admission after abrupt cessation of cocaine use. Almost all symptoms decreased over the ensuing 3 weeks, and there were statistically significant declines in the subjective ratings of craving, drug withdrawal, physical discomfort, anxiety, and depression. Nonspecific emotional distress on admission was suggested by the decrease over time of seemingly contradictory affective states (e.g., calm and anxious). Similarly, the nurses' ratings of depression and anxiety, which remained at modest levels throughout, showed some increase over time. This seemed to reflect increasing apprehension and discouragement at the prospect of returning to the circumstances that had prompted hospitalization. Contradictory sensory abnormalities (e.g., hyperesthesia and hypesthesia) were also reported as improved, although some of these (e.g., hyperosmia and hyposmia) undoubtedly reflected local effects of cocaine. The greatest declines in symptoms occurred during the first week after admission, although there was considerable variability among patients. At no point during the study did any patient

meet the *DSM-III-R* criteria for a major axis I disorder other than cocaine withdrawal. The patients' mean plasma prolactin level did not differ at baseline from the normal subjects' level, but it showed a small but significant increase over the ensuing 3 weeks. The plasma GH and HVA levels did not change significantly, nor did the GH level differ from that of the normal subjects. These results are consistent with previous findings that cocaine addicts' levels of plasma prolactin (14, 15) and GH (15) during early abstinence do not differ from those of normal subjects. However, prolactin levels that were higher (9–12) and lower (13) than normal have also been reported, and our observation of an increase in prolactin over time corresponds with the former finding; high GH levels have also been reported (13). Given the many factors that might produce prolactin changes of this magnitude, these observations should be viewed as consistent with, but not confirmatory of, abnormal central dopamine function. Unlike Martin et al. (23), we found no relationship between HVA or prolactin and self-reported craving.

This study failed to demonstrate the emergence of phasic clinical phenomena after cessation of heavy cocaine use (5). In contrast, these findings are highly consistent with those of Weddington et al. (8), who reported steady and significant declines in symptoms over several weeks of abstinence. The present study did not include a comparison group of hospitalized normal subjects to permit evaluation of the severity of baseline symptoms. However, clinical impressions and the rating scale data indicated that most patients experienced relatively mild symptoms.

Interpretation of these findings is subject to many of the methodological considerations discussed by Weddington et al. (8), since the designs of the two studies are similar. Most important, the subjects in both studies were hospitalized. Exposure to environmental and interoceptive cues associated with drug use differs markedly between inpatient and outpatient settings, and it is well established that withdrawal phenomena are affected by conditioned responses to such cues (24). This factor may partly account for the failure of these studies to support the phasic model of cocaine withdrawal, which was based exclusively on observations of outpatients (5). Alternatively, it is possible that the initial "crash" postulated in the phasic model was not observed in these patients because it occurred before hospital admission. Whether a phasic model accurately describes the course of symptoms after cessation of cocaine addiction for outpatients remains to be established.

This study confirms the impression of Weddington et al. (8) that the symptoms following inpatient cessation of uncomplicated cocaine addiction are relatively mild and decrease linearly over the first month. These findings do not support the routine use of pharmacological agents in the inpatient management of recently abstinent cocaine addicts (25). The clinical and neurobiological implications of the modest neuroendocrine abnormalities we observed remain to be clarified.

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The Frequency of Multiple Personality Disorder Among Psychiatric Inpatients

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Objective: A 2-year study was undertaken to determine the frequency of multiple personality disorder among general adult psychiatric inpatients. **Method:** All individuals admitted to two 23-bed acute care wards in a teaching hospital in Winnipeg, Man., were screened with the Dissociative Experiences Scale. Individuals with prior diagnoses of multiple personality disorder were excluded. All subjects scoring 20 or higher on the Dissociative Experiences Scale were interviewed with the Dissociative Disorders Interview Schedule. Then subjects with a diagnosis of multiple personality disorder and comparison subjects were interviewed by a clinician who was blind to all research data. **Results:** A total of 299 subjects completed the Dissociative Experiences Scale and 80 received a structured diagnostic interview. Ten subjects (3.3%) had clinically confirmed multiple personality disorder. **Conclusions:** If these results are replicated and accepted, multiple personality disorder will become a serious consideration in the differential diagnosis of many psychiatric patients.

(Am J Psychiatry 1991; 148:1717-1720)

There has been renewed interest in the dissociative disorders, especially multiple personality disorder, since 1980 (1-4). Several reports have suggested that multiple personality disorder is much more common on psychiatric inpatient units than was previously suspected. Putnam and associates (5) diagnosed three cases of multiple personality disorder in about 225 psychiatric inpatients, and Bliss and Jeppsen (6) made the diagnosis in 16% of 50 inpatients. Ross (7) diagnosed multiple personality disorder in 4.4% of 68 inpatients admitted to a general adult inpatient unit over a year. Saxe and co-workers (8) found two cases (3.3%) of multiple personality disorder and 10 patients with other dissociative disorders in a group of 60 general adult inpatients.

These are the only reports of the frequency of multiple personality disorder among psychiatric inpatients. Setting aside the study by Bliss and Jeppsen, the frequency of multiple personality disorder among general

adult psychiatric inpatients in reports to date ranges from 1% to 5%.

Screening studies have reported multiple personality and other dissociative disorders in a variety of clinical and nonclinical populations including patients at a community mental health center (9), prostitutes and exotic dancers (10), sexual abuse survivors (11), chemical dependency patients (12), and the general population (13). Loewenstein (14) has reviewed the literature on psychogenic amnesia and psychogenic fugue, noting the frequent occurrence of these disorders among combat troops.

To our knowledge, the present study is the first systematic screening of a large group of psychiatric inpatients for multiple personality disorder through use of a valid and reliable structured interview and blind clinical assessments.

METHOD

Subjects

Subjects for the study were all individuals admitted to two 23-bed general adult psychiatric inpatient units at a university teaching hospital in Winnipeg, Man., over a 2-year period from July 18, 1988, to July 17, 1990. Patients with a diagnosis of multiple personality disorder made before admission were excluded. All individuals admitted during this period were approached and asked to participate in the study. All those agreeing to participate gave written consent; permission to ap-

Presented at the Seventh Annual International Conference on Multiple Personality/Dissociative States, Chicago, Nov. 9, 1990. Received Jan. 25, 1991; revision received May 15, 1991; accepted June 14, 1991. From the Department of Psychiatry, University of Manitoba, the Department of Psychiatry, St. Boniface Hospital, and the Department of Psychology, University of Winnipeg, Winnipeg, Man. Dr. Ross's address is Charter Hospital Dallas, 6800 Preston Rd., Plano, TX 75024. Reprints of this article are not available.

Supported by grants from the Manitoba Mental Health Research Foundation and the Manitoba Health Research Council.

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proach the subjects had been obtained from the psychiatrists admitting patients to the units. The 20 comparison subjects were drawn from the same patient population. Ethical approval for the project was received from the university's faculty committee on the use of human subjects in research.

Procedure

The study was conducted in three phases. In the first phase, all subjects were approached and asked to complete the Dissociative Experiences Scale (15). The Dissociative Experiences Scale is a 28-item self-report measure that takes 5–10 minutes to complete. It yields an overall score ranging from 0 to 100; scores above 20 suggest the presence of posttraumatic stress disorder or a dissociative disorder. The Dissociative Experiences Scale has a test-retest reliability of 0.84 and good split half reliability (15). Group median scores on the scale discriminate subjects with multiple personality disorder from other diagnostic groups and normal comparison subjects (15, 16). General population norms for the scale are available (17, 18).

In the second phase of the study all subjects who scored 20 or higher on the Dissociative Experiences Scale were interviewed with the Dissociative Disorders Interview Schedule. A cutoff score of 20 was chosen because scores above 20 are suggestive of a dissociative disorder (1, 2, 15, 16). The Dissociative Disorders Interview Schedule is a structured interview that makes *DSM-III-R* diagnoses of somatization disorder, major depressive episode, borderline personality disorder, and all the dissociative disorders (2, 19, 20). The schedule has an overall interrater reliability of 0.68 and good validity for the diagnosis of multiple personality disorder. In its original development the interview was administered to 80 subjects, of whom 20 had multiple personality disorder (21). Cohen's kappa (22) for agreement between clinician and structured interview for the diagnosis of multiple personality disorder among these 80 subjects was 0.95. The schedule can discriminate subjects with multiple personality disorder from a number of other diagnostic groups (21, 23). The full text of the Dissociative Disorders Interview Schedule is available in two sources (2, 20).

In the third phase of the study all subjects with a diagnosis of multiple personality disorder according to the Dissociative Disorders Interview Schedule and comparison subjects without a diagnosis of multiple personality according to structured interview were given a clinical diagnostic interview by a clinician (W.P.F.) who was blind to their clinical diagnoses and all research data. The clinician did not know the exact ratio of multiple personality to comparison subjects. The comparison subjects all scored 20 or higher on the Dissociative Experiences Scale and had completed the structured interview. Because the comparison subjects had experienced numerous dissociative phenomena, they presented difficult problems in differential diagnosis. All comparison subjects were matched to a patient with

multiple personality disorder by gender and age (within 10 years).

Data Analysis

The age, gender, length of stay, and discharge clinical diagnosis were tabulated for each individual admitted. Subjects who completed the Dissociative Experiences Scale were compared to those who did not complete the scale to determine whether the two groups differed on gender or age; two-tailed *t* tests were used for these analyses.

The frequency of multiple personality disorder was calculated on the basis of the number of subjects who received a confirming clinical diagnosis from a clinician. In addition, the total number of subjects who received at least one dissociative disorder diagnosis on the Dissociative Disorders Interview Schedule was calculated.

RESULTS

During the 2-year period of the study, 484 individuals were admitted to the two wards, excluding patients previously diagnosed as having multiple personality disorder. Their mean age was 41.8 years (range=18–80 years), and 61.6% were women. The average length of stay was 37 days. The percentages of subjects with various discharge diagnoses were as follows: personality disorder, 31.0% (*N*=150); bipolar disorder, 23.8% (*N*=115); other mood disorders, 25.4% (*N*=123); psychotic disorder not elsewhere classified, 14.5% (*N*=70); schizophrenia, 14.3% (*N*=69); substance abuse, 9.1% (*N*=44); and organic mental disorder, 5.8% (*N*=28).

Of the 484 subjects, 299 (61.8%) completed the Dissociative Experiences Scale. Women made up 62.1% of those who completed the scale and 61.6% of those who did not complete the scale; this difference was not significant (*t*=0.1, *df*=481, *n.s.*). The mean±SD age of the subjects who completed the scale was 40.1±15.9 years, compared to a mean age of 44.6±17.8 years for those who did not complete the scale (*t*=2.9, *df*=476, *p*<0.004). Variations in degrees of freedom for these analyses are due to missing data. Reasons for not completing the Dissociative Experiences Scale were patient refusal (*N*=80), poor concentration (*N*=48), organic disorder (*N*=5), patient not contacted before discharge (*N*=41), and other (*N*=11).

Of the 299 subjects who completed the Dissociative Experiences Scale, 90 (30.1%) scored 20 or higher. The mean scale score was 14.6±14.2, and the median score was 9.1.

Eighty subjects completed the Dissociative Disorders Interview Schedule. Of these, 47 (58.8%) had a diagnosis of borderline personality disorder; 12 (15.0%), somatization disorder; 72 (90.0%), major depressive episode; and 62 (77.5%), a dissociative disorder. Ten subjects scoring above 20 on the Dissociative Experiences Scale either refused further participation in the study or could not be interviewed before discharge.

Sixteen subjects (5.4%) received a *DSM-III-R* clinical diagnosis of multiple personality disorder. These 16 subjects included 10 (3.3%) who received a diagnosis of multiple personality disorder on the Dissociative Disorders Interview Schedule and from the blind study clinician; three who received a clinical diagnosis of multiple personality disorder from the study clinician but a diagnosis of some other dissociative disorder on the Dissociative Disorders Interview Schedule; and three who received diagnoses of multiple personality disorder from attending clinicians not participating in the study, on the basis of direct contact with alter personalities, and diagnoses of some other dissociative disorder on the Dissociative Disorders Interview Schedule. Of these last three subjects, only one was interviewed by the study clinician, who made a diagnosis of bipolar mood disorder.

DISCUSSION

On the basis of this study, the conservative estimate of the frequency of multiple personality disorder among general adult inpatients is 3.3%. This is the percentage of subjects who received the diagnosis from both the Dissociative Disorders Interview Schedule and the study clinician. However, an additional six patients received definite clinical diagnoses of multiple personality disorder, for a total of 16 (5.4%). Given that about 15% of clinically diagnosed patients with multiple personality disorder score below our cutoff score of 20 on the Dissociative Experiences Scale, we feel that 5% is a realistic minimum round figure for the frequency of multiple personality disorder on general adult psychiatric inpatient units.

Of the 80 subjects interviewed with the Dissociative Disorders Interview Schedule, 62 had a dissociative disorder of some kind. Although most of these diagnoses were not validated, these 62 patients represent 20.7% of the total number of subjects in the study, which suggests that dissociative disorders are common among inpatients.

Previous studies of the frequency of multiple personality disorder among psychiatric inpatients have not used a reliable structured interview or blind clinical interviews of patients with multiple personality disorder and comparison subjects. They were, therefore, subject to observer bias. Despite such possible bias, with the exception of Bliss and Jeppsen's study (6), the frequency of multiple personality disorder on inpatient units has been consistently in the range of 1%–5% (5–8). It is not possible to determine from the methodology reported in Bliss and Jeppsen's paper whether their higher rate of multiple personality disorder was due to demand characteristics, use of hypnosis and hypnotic profiles, or other factors or whether it was accurate.

The main reason that multiple personality disorder is not diagnosed frequently on inpatient units is probably because all of the symptom clusters, especially the secondary features of multiple personality disorder, are

not inquired about systematically on a routine basis. In terms of practical constraints on clinical time, the secondary features of multiple personality disorder, which are listed in a previous publication (19), can be inquired about in a few minutes.

Are there any methodological limitations to our study which call into question the finding that multiple personality disorder affects at least 5% of psychiatric inpatients? There is no reason to think that our inpatient population differs markedly from other teaching hospital patient populations, although, of course, results cannot be generalized to all of North America. None of the patients in the study was brought to our emergency department for admission because of our interest in dissociative disorders; of the 16 subjects with clinically confirmed multiple personality disorder, the first author was attending physician for only six.

Although there was a statistically significant difference in age between those subjects who completed the Dissociative Experiences Scale and those who did not, we do not think that this difference of 4 years is clinically significant. There is, therefore, no evidence of a clinically significant sampling bias.

The validity of the study hinges on the validity of the clinical diagnoses, which we believe were correct. Even if some of the diagnoses were false positives, however, those subjects surely suffer from a dissociative disorder of some type, so the finding that dissociative disorders appear to be common among psychiatric inpatients would still hold.

In summary, the present study, which requires replication, suggests that multiple personality disorder is relatively common on general adult inpatient units, affecting at least 5% of individuals admitted. Multiple personality disorder will not be diagnosed very often unless a specific inquiry regarding its features is made part of daily clinical practice. If this finding is replicated and accepted, it will result in a shift in our thinking about multiple personality disorder. Multiple personality disorder will become a serious consideration in the differential diagnosis of a considerable number of psychiatric inpatients and, by extension, of patients seen in other settings including emergency departments. The dissociative disorders should be inquired about routinely in psychiatric assessments.

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Psychiatric Status of Patients With Primary Fibromyalgia, Patients With Rheumatoid Arthritis, and Subjects Without Pain: A Blind Comparison of *DSM-III* Diagnoses

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Objective: The major purpose of this study was to compare the frequency of the occurrence of *DSM-III* diagnoses in patients with primary fibromyalgia syndrome, patients with rheumatoid arthritis, and subjects without pain. **Method:** Thirty-five patients with primary fibromyalgia, 33 patients with rheumatoid arthritis, and 31 nonpatients without pain were blindly assessed for psychiatric diagnoses with the Psychiatric Diagnostic Interview. **Results:** Data from this interview revealed no group differences in terms of lifetime history of any psychiatric disorders, including major depression, somatization disorder, or anxiety-based disorders. Analysis of the auxiliary symptoms of depression on the Psychiatric Diagnostic Interview revealed that the patients with fibromyalgia did not report a higher frequency of vegetative signs of depression. However, analysis of the somatization scale revealed an interaction between medical and psychiatric diagnoses: patients with primary fibromyalgia syndrome and a psychiatric history endorsed significantly more somatic symptoms than did patients with rheumatoid arthritis or subjects without pain, and fibromyalgia patients without a psychiatric history were no more likely to endorse somatic symptoms than were arthritis patients or subjects without pain. **Conclusions:** The Psychiatric Diagnostic Interview data failed to discriminate in any major way between primary fibromyalgia syndrome (a disorder with no known organic etiology) and rheumatoid arthritis (a disorder with a known organic etiology). Therefore, these data do not support a psychopathology model as a primary explanation of the symptoms of primary fibromyalgia syndrome.

(*Am J Psychiatry* 1991; 148:1721-1726)

Primary fibromyalgia syndrome is characterized by generalized aches, pains, tender points, stiffness, and fatigue (1). Despite increasing recognition of this syndrome as a clinical entity (1, 2), its etiology remains obscure. The lack of a definitive pathophysiology has led several investigators to examine the role of psychological/psychiatric factors in the presentation of symptoms associated with primary fibromyalgia syndrome (3-11). The initial studies relied primarily on paper-and-pencil psychological inventories such as the MMPI. Two general patterns of results have emerged: 1) studies that have found differences between patients with primary fibromyalgia syndrome and control subjects, such as pa-

tients with rheumatoid arthritis, have also found that the percentage of patients with substantial psychological symptoms is relatively low (18%-41%) (4, 5), and 2) other studies have found no differences between groups with primary fibromyalgia syndrome and rheumatoid arthritis on a variety of psychological measures (6, 8, 9). Taken together, these studies have not provided strong support for a psychopathology model to explain the symptoms of primary fibromyalgia syndrome. However, none of these studies provided data relevant to the frequency of formal psychiatric diagnoses among patients with primary fibromyalgia syndrome.

Two studies (10, 11) and one case series (12) examined the occurrence of *DSM-III* diagnostic categories in patients with primary fibromyalgia syndrome and rheumatoid arthritis (10, 11). Hudson et al. (10) found a significantly higher occurrence of a history of major depression (71%) in fibromyalgia patients than in arthritis patients (13%), and Tariot et al. (12) reported that six of seven fibromyalgia patients had a current or previous history of depression. However, Kirmayer et al. (11) found no significant differences in the occur-

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rence of depression between fibromyalgia patients (20%) and arthritis patients (8.7%).

Kirmayer et al. (11) proposed both methodological and sample characteristic differences that may have explained the discrepancies between their findings and those of Hudson et al. (10) and Tariot et al. (12). Additionally, all three reports contain potential methodological difficulties that may have influenced the pattern of results: 1) a small sample size in certain groups (e.g., Hudson et al. [10] had only 14 patients with rheumatoid arthritis as a comparison group, and Tariot et al. [12] studied only seven fibromyalgia patients), 2) no study described specific steps to ensure the blinding of the psychiatric interviewer to medical diagnosis, 3) no study examined the reliability of psychiatric diagnoses, and 4) no study controlled for differences in the severity of pain between patients with primary fibromyalgia syndrome and patients with rheumatoid arthritis. The latter point is important because there are data to suggest that patients with primary fibromyalgia syndrome report more severe pain than patients with rheumatoid arthritis (13). Therefore, the prevalence of psychiatric disorders (especially depression) may have been confounded by differences in pain intensity.

The purpose of the present study was, first, to examine the occurrence of *DSM-III* psychiatric disorders in patients with primary fibromyalgia syndrome, patients with rheumatoid arthritis, and subjects without pain while correcting for the methodological issues just described. Secondly, we were interested in the tendency of patients with primary fibromyalgia syndrome to endorse psychiatrically relevant symptoms. Two studies (9, 11) have reported that patients with primary fibromyalgia syndrome tend to endorse a wider variety of somatic symptoms than do patients with rheumatoid arthritis. On the other hand, Kirmayer et al. (11) reported that fibromyalgia patients, as a group, did not differ from arthritis patients in the endorsement of vegetative signs of depression, thereby arguing against a masked depression hypothesis. However, neither study compared symptom reporting in fibromyalgia patients and/or arthritis patients with and without psychiatric diagnoses. Therefore, we were interested in examining the interaction between medical and psychiatric diagnoses and the tendency to endorse psychiatrically relevant symptoms. Specifically, we reasoned that support for the hypothesis that primary fibromyalgia syndrome is a variant of masked depression or another psychiatric spectrum disorder would be found if patients with primary fibromyalgia syndrome and no psychiatric history endorsed more psychiatrically relevant symptoms than either patients with rheumatoid arthritis or subjects without pain.

METHOD

Thirty-five patients with primary fibromyalgia syndrome, 33 patients with rheumatoid arthritis, and 31 nonpatients without pain made up the study group.

There were 30 women and five men in the fibromyalgia group; their mean \pm SD age was 42.8 \pm 9.2 years. There were 32 women and one man in the arthritis group; their mean age was 46.9 \pm 9.0 years. There were 31 women and no men in the group of nonpatients without pain; their mean age was 44.9 \pm 13.9 years.

The fibromyalgia patients were diagnosed by using the Yunus criteria (1), and the arthritis patients satisfied the American Rheumatism Association criteria for classic or definite rheumatoid arthritis (14). The nonpatients had no substantial pain or medical problems and were recruited from friends and neighbors of the fibromyalgia patients to control for socioeconomic status. A one-way analysis of variance (ANOVA) revealed no significant differences in age and a chi-square analysis revealed no differences in the distribution of men and women among the three groups.

The fibromyalgia patients had been ill for 9.4 \pm 8.1 years (range=0.5–42 years), and the arthritis patients had been ill for 5.9 \pm 6.0 years (range=0.2–32 years). A *t* test comparison failed to show a significant difference in the duration of symptoms between the two groups of patients.

Following an explanation of the study and signing of informed consent forms, participants were interviewed by a psychiatrist (S.A.K. or D.A.S.) or a clinical psychologist (T.A.A.) using the Psychiatric Diagnostic Interview (15), a structured interview for deriving *DSM-III* diagnoses for 12 psychiatric disorders (organic brain syndrome, alcoholism, drug dependency, mania, depression, schizophrenia, antisocial personality disorder, somatization disorder, anorexia nervosa, obsessive-compulsive disorder, phobia, and panic disorder). The Psychiatric Diagnostic Interview was chosen over the Schedule for Affective Disorders and Schizophrenia (16) or the National Institute of Mental Health Diagnostic Interview Schedule (17) for four reasons. First, evidence supports the reliability and validity of the Psychiatric Diagnostic Interview (15). Second, the Psychiatric Diagnostic Interview has been shown to discriminate between medical and psychiatric populations (18). Third, because the diagnostic criteria of the Psychiatric Diagnostic Interview are more stringent than those of *DSM-III*, subjects who qualify for a diagnosis according to this interview will definitely qualify for a *DSM-III* diagnosis. Finally, because the Psychiatric Diagnostic Interview takes less time to administer it is more practical for use in clinical research.

To ensure that the interviewers were blind to the subject's medical diagnosis (especially in the case of patients with rheumatoid arthritis, where inspection of the patients' joints or observation of their gait may reveal pathognomonic signs), the following steps were taken. First, the patient was conducted to the interview room by a member of the support staff so that when the interviewer went to meet the patient, he or she was already seated behind a desk. Thus, the interviewer did not see the patient walking. Second, the patient was given two pairs of gloves to wear—a sterile surgical pair that was later discarded and a large pair of garden

TABLE 1. Frequency of Lifetime Psychiatric Diagnoses in Patients With Primary Fibromyalgia Syndrome or Rheumatoid Arthritis and Nonpatients Without Pain

Lifetime Psychiatric Diagnosis	Patients With Primary Fibromyalgia Syndrome (N=35)		Patients With Rheumatoid Arthritis (N=33)		Subjects Without Pain (N=31)	
	N	%	N	%	N	%
Any psychiatric disorder	17	48.6	19	57.6	11	35.5
Major depression	12	34.3	13	39.4	8	25.8
Somatization disorder	4	11.4	1	3.0	0	0.0
Phobia	6	17.1	7	21.2	4	12.9
Panic disorder	5	14.3	2	6.1	1	3.2
Obsessive-compulsive disorder	2	5.7	1	3.0	0	0.0

gloves. This prevented the interviewer from observing any joint deformities in the hands. Third, the patient was instructed to make no reference at all to his or her medical diagnosis.

All interviews were audiotaped and independently rescored, yielding a kappa coefficient of 0.86. (For the calculation of kappa, an agreement on diagnosis meant that each rater agreed on the presence of all diagnoses for an individual.) For the seven subjects (three fibromyalgia patients, three arthritis patients, and one subject without pain) for whom disagreements arose, the interviewer and the reviewer listened to the tape of the session together and arrived at a consensus regarding diagnosis.

Finally, all subjects completed the Pain Mannequin (19, 20), which consists of a schematic drawing of the body on which the intensity of "aches and pains" of 25 body areas is rated on an 11-point scale on which 0=no aches or pain and 10=extreme pain. The number of non-0 ratings (i.e., the total number of pain sites) represents the pain frequency score, and the sum of the ratings represents the total pain score.

RESULTS

Because significant differences in the number of body areas affected by pain and/or differences in the intensity of pain between the patients with primary fibromyalgia syndrome and those with rheumatoid arthritis could have confounded the results of the present study, the Pain Mannequin data were analyzed first. One-way ANOVAs revealed significant main effects for the pain frequency score ($F=22.2$, $df=2$, 92, $p<0.001$) and total pain score ($F=21.2$, $df=2$, 92, $p<0.001$). However, in each case, post hoc analyses with the Newman-Keuls multiple range test revealed that fibromyalgia patients and arthritis patients differed significantly from the subjects without pain but did not differ from each other. The mean pain frequency score of the fibromyalgia patients was 14.2 ± 7.9 , that of the arthritis patients was 11.6 ± 10.3 , and that of the subjects without pain was 1.9 ± 2.5 . The mean total pain score of the fibromyalgia patients was 48.7 ± 36.2 , that of arthritis patients was 41.2 ± 33.5 , and that of subjects without pain was 4.4 ± 6.2 .

Table 1 describes the frequency of lifetime diagnosis of any psychiatric disorder, major depression, somati-

zation disorder, and anxiety-based disorders. To make our data comparable with the data of Hudson et al. (10), these data represent the percentages of all psychiatric disorders even if a masking or preemptive diagnosis was also present. Chi-square analysis revealed no significant differences among the three groups in terms of the frequency of any psychiatric diagnosis, major depression, somatization disorder, or anxiety-based disorders. Of note, however, is the prevalence of somatization disorder in the fibromyalgia patients (11.4%). Although not statistically significant in the current study group, the percentage is appreciably higher than expected from population surveys (21).

As stated in the Method section, the Psychiatric Diagnostic Interview criteria tend to be more stringent than *DSM-III* criteria. Major depression and somatization disorder are the diagnoses where this difference could significantly influence the data of the current study. For depression, the required duration of depressive symptoms for the Psychiatric Diagnostic Interview is 1 month, compared with 2 weeks for *DSM-III*. If the *DSM-III* 2-week criterion is used, 15 (42.9%) of the fibromyalgia patients, 13 (39.4%) of the arthritis patients, and eight (25.8%) of the subjects without pain had major depression. For somatization disorder, the Psychiatric Diagnostic Interview requires the presence of at least 25 of 69 symptoms, but *DSM-III* requires a minimum of 13 of 35 symptoms. If the *DSM-III* requirement is used, one additional fibromyalgia patient and one additional arthritis patient met criteria for somatization disorder. Although more patients were diagnosed as having depression and somatization disorder when the *DSM-III* criteria were used, chi-square analysis again revealed no significant group differences.

Although the distribution of men was not statistically different among the groups, a systematic difference among men (e.g., if none of them had psychiatric diagnoses) could have masked important differences. Of the six men in the study, three (two with primary fibromyalgia syndrome and one with rheumatoid arthritis) met criteria for one or more psychiatric disorders, including depression ($N=2$), phobia ($N=2$), panic ($N=1$), mania ($N=1$), and drug abuse ($N=1$). Therefore, the frequency of psychiatric disorders and the types classified do not suggest systematic differences between men and women.

To examine the tendency of patients with primary fibromyalgia syndrome to report psychiatrically relevant

TABLE 2. Symptoms Endorsed on the Depression and Somatization Scales of the Psychiatric Diagnostic Interview by Patients With Primary Fibromyalgia Syndrome or Rheumatoid Arthritis and Nonpatients Without Pain

Subjects	Symptoms Endorsed on the Psychiatric Diagnostic Interview Scale			
	Depression ^a		Somatization	
	Mean	SD	Mean	SD
Primary fibromyalgia syndrome (N=35)				
Psychiatric diagnosis (N=17) ^b	13.6	6.5	15.6	10.9
No psychiatric diagnosis (N=18)	0.8	2.1	3.7	7.0
Patients with rheumatoid arthritis (N=33)				
Psychiatric diagnosis (N=19) ^c	11.6	6.4	8.1	9.6
No psychiatric diagnosis (N=14)	1.2	2.8	1.2	2.9
Nonpatients without pain (N=31)				
Psychiatric diagnosis (N=11)	9.8	6.7	1.5	4.0
No psychiatric diagnosis (N=20)	0.1	0.4	0.9	2.6

^aPatients with a psychiatric diagnosis differed significantly from those with no psychiatric diagnosis ($F=110.2$, $df=1, 93$, $p<0.001$).

^bPatients with primary fibromyalgia syndrome and a psychiatric history endorsed significantly more somatization symptoms than any other group ($p<0.05$, post hoc Newman-Keuls).

^cPatients with rheumatoid arthritis and a psychiatric history endorsed significantly more somatization symptoms than all other groups except patients with primary fibromyalgia syndrome and a psychiatric history ($p<0.05$, post hoc Newman-Keuls).

symptoms, a three-by-two ANOVA was done with the auxiliary symptoms (those used to make a diagnosis) from the depression and somatization scales of the Psychiatric Diagnostic Interview as dependent measures and medical diagnosis (primary fibromyalgia syndrome, rheumatoid arthritis, no pain) and the presence or absence of a psychiatric diagnosis as grouping variables (table 2). Analysis of the depression scale revealed a main effect for psychiatric diagnosis: patients with a psychiatric diagnosis admitted to more symptoms of depression (table 2). Analysis of the somatization scale revealed a significant effect for the interaction term ($F=6.9$, $df=2, 93$, $p<0.002$). Post hoc analysis with the Newman-Keuls multiple range test revealed that 1) in the absence of a psychiatric diagnosis, there were no significant differences among the fibromyalgia patients, arthritis patients, and subjects without pain and 2) in the presence of a psychiatric disorder, the fibromyalgia patients reported significantly more auxiliary symptoms of somatization than either the arthritis patients or the subjects without pain, and the arthritis patients reported significantly more than the subjects without pain (table 2).

This analysis could have been confounded by the presence of four patients with primary fibromyalgia syndrome and somatization disorder because, by definition, these patients admit to an inordinate number of symptoms. Therefore, the analysis was repeated with

patients who met criteria for somatization disorder removed (four fibromyalgia patients and one patient with rheumatoid arthritis). This secondary analysis revealed an identical pattern of results.

DISCUSSION

The Psychiatric Diagnostic Interview data revealed no significant differences between patients with primary fibromyalgia syndrome, patients with rheumatoid arthritis, and subjects without pain in terms of the frequency of lifetime diagnosis of any psychiatric disorder, major affective disorder, somatization disorder, or anxiety-based disorders. This pattern of results is consistent with the data of Kirmayer et al. (11) and appears more consistent with the rate of depression reported in Goldenberg's extension (22) of the study of Hudson et al. (10). Kirmayer et al. (11) suggested that the original study of Hudson et al. (10) may have been biased by sampling error. Unfortunately, Goldenberg (22) did not report an extended series of arthritis patients; therefore, we do not know if the significantly higher rate of depression in fibromyalgia patients than in arthritis patients would have been maintained.

Further, analysis of the auxiliary symptoms of depression revealed a main effect for psychiatric diagnosis only. Patients with primary fibromyalgia syndrome had no more tendency to admit to vegetative signs of depression than either the patients with rheumatoid arthritis or the subjects without pain, which is also consistent with the data of Kirmayer et al. (11). Therefore, these data are not consistent with the hypothesis that primary fibromyalgia syndrome is a form of masked depression. However, this study was not specifically designed to diagnose masked depression; therefore, it is possible that the use of criteria other than vegetative signs would produce significant group differences.

The prevalence of somatization disorder in patients with primary fibromyalgia syndrome (11.4%), although not statistically different from the prevalence in patients with rheumatoid arthritis and the subjects without pain, appears quite high compared with prevalence rates from population surveys (21). Additionally, when we examine the prevalence of somatization disorder in the women studied in the current report and in the reports of Hudson et al. (10) and Kirmayer et al. (11), we find that eight (10.5%) of 76 patients with primary fibromyalgia syndrome versus two (3.4%) of 59 patients with rheumatoid arthritis met DSM-III criteria for somatization disorder (Kirmayer et al. did not specify the gender of the patient with somatization disorder; however, we assumed it was a woman). If this pattern were seen in a larger study, the difference in the frequency of somatization disorder in fibromyalgia patients, compared with arthritis patients and subjects without pain, would likely be significant. An interesting empirical question that would arise from such a finding would be whether the higher frequency of somatization disorder in fibromyalgia patients represents an associa-

tion between the two disorders or a bias in referral patterns. In other words, are patients with somatization disorder, who would likely meet criteria for many medical syndromes (including primary fibromyalgia syndrome, migraine headache, irritable bowel syndrome, and myofascial pain), more likely to be referred to rheumatologists known to be interested in studying primary fibromyalgia syndrome?

On the other hand, analysis of the auxiliary symptoms from the somatization scale revealed a significant interaction between medical and psychiatric diagnoses even when patients with formal somatization disorder were removed. The pattern of results indicates that patients with primary fibromyalgia syndrome and no psychiatric history are no different from patients with rheumatoid arthritis or subjects without pain in terms of endorsing somatic symptoms of unknown organic etiology. However, in the presence of a psychiatric history, fibromyalgia patients endorsed significantly more somatic symptoms than did arthritis patients or subjects without pain. Interestingly, the arthritis patients with a psychiatric history also tended to endorse more somatic symptoms, although to a lesser extent, than the fibromyalgia patients. These data support the proposal of Turk and Flor (23) that there are subgroups of fibromyalgia patients with different clinical presentations.

The precise explanation for this pattern of results cannot be identified from the current data. However, several authors have proposed that symptom reporting in certain patients with ambiguous physical findings may be related to a tendency to attend to and amplify normal bodily sensations (19, 24). This type of model may be particularly relevant for the group of patients with primary fibromyalgia syndrome and psychiatric diagnoses.

On the whole, we believe that the most parsimonious interpretation is that the Psychiatric Diagnostic Interview data failed to discriminate in any major way between groups with primary fibromyalgia syndrome (a disorder with no known organic etiology) and rheumatoid arthritis (a disorder with a known organic etiology). Therefore, these data do not support a psychopathology model as a primary explanation of the symptoms of fibromyalgia. However, the presence of a psychiatric disorder is relevant in that patients with primary fibromyalgia syndrome and a psychiatric history endorsed significantly more somatic symptoms. Additionally, these data do not rule out the possibility that there are other psychological factors that are important in the development and maintenance of primary fibromyalgia syndrome.

On a larger scale, this study, as well as our previous research (4-6), does not support the hypothesis that pain in the absence of an organic etiology is a variant of a psychiatric disorder such as depression or masked depression (25). These results are not surprising if one reviews the larger pain literature. Numerous studies have attempted to discriminate between pain patients with and without a known organic etiology for the pain based on psychological/psychiatric symptoms. The ma-

jority of these studies have failed to discriminate between groups (26). Additionally, patients with primary fibromyalgia syndrome are not unique in having no clear pathophysiology to explain their pain. Many patients with disorders such as low back pain and tension headache have no known organic basis for the presentation of their painful symptoms. Therefore, rather than viewing primary fibromyalgia syndrome from either a medical or psychiatric model, we believe that future researchers should take the example of work with other pain syndromes and develop multidimensional models of primary fibromyalgia syndrome which include physiological, affective, cognitive, behavioral, and social components (23).

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Seasonal Variation in Obsessive-Compulsive Disorder: Preliminary Experience With Light Treatment

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The authors surveyed 34 patients with obsessive-compulsive disorder for a history of seasonal variations in symptoms and behavior and treated six of these patients with bright light. Overall, the patients with obsessive-compulsive disorder did not report a greater degree of seasonal variations than normal and no response was seen to bright light therapy in the small number of patients treated.

(Am J Psychiatry 1991; 148:1727-1729)

There has been increasing interest recently in seasonal variation in psychiatric symptoms following the description of seasonal affective disorder (1), which responds to treatment with bright artificial light (2). It has become apparent that light therapy may also be therapeutic for other conditions, including nonseasonal depressions (3), premenstrual syndrome (4), and delayed sleep-phase syndrome (5). It would be useful to explore to what degree seasonality might be a feature of other neuropsychiatric conditions as well as the scope of therapeutic efficacy of light therapy in such conditions.

In the present study, we investigated seasonal variation in symptoms of 34 patients with obsessive-compulsive disorder and conducted a pilot study on the effect of light treatment in six of these patients.

METHOD

The subjects were 34 patients of the obsessive-compulsive clinic at the National Institute of Mental Health

(NIMH) between November 1989 and February 1990. The patients included 17 men and 17 women; their mean \pm SD age was 36.9 \pm 10.5 years. All patients met DSM-III-R criteria for obsessive-compulsive disorder as determined by two independent psychiatrists, and all had exhibited symptoms for at least 1 year and had NIMH Global Obsessive-Compulsive Rating Scale scores greater than 4 on a scale of 1-15 (4=at least 1 hour a day of obsessive-compulsive symptoms). All patients were medically healthy, as determined by normal physical examination results and routine laboratory test results.

All patients were given the Seasonal Pattern Assessment Questionnaire (6), a self-administered instrument for evaluating seasonal mood and behavior changes retrospectively. This questionnaire provides 1) scores for seasonal variation in length of sleep, social activity, mood, weight, and appetite and energy levels (the sum of these scores provides a global seasonality score), 2) best and worst months for these behaviors, and 3) the degree to which these changes are experienced as a problem. The Seasonal Pattern Assessment Questionnaire has been shown to have reasonable test-retest reliability (7, 8) and to discriminate between different clinical and normal populations (7, 8). Extra items, asked in the same manner as the regular items, were added to evaluate seasonal variation in obsessive-compulsive symptoms retrospectively. These items, available on request from one of us (N.E.R.), have not yet been validated.

Of the 34 subjects, all who met the following criteria were asked to participate in an open study of light ther-

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The authors thank Suzanne Bernstein, B.A., and Gay Grover, M.S.N., for their assistance.

apy: 1) not involved in active research protocols, 2) scored higher than 4 on the NIMH Global Obsessive-Compulsive Rating Scale, and 3) if receiving medications, on a stable dose for at least 3 months. Six patients fulfilled these criteria and were given phototherapy. Four of these were women and two were men; their mean \pm SD age was 35.5 \pm 7.2 years. Their mean \pm SD duration of symptoms was 22.8 \pm 8.6 years. Four were receiving clomipramine at doses of 100–175 mg/day, two in combination with 60 mg/day of buspirone; one was receiving 80 mg/day of fluoxetine; and one was unmedicated. Their predominant obsessive-compulsive symptoms were checking behaviors (five patients), fear of harming others (three patients), excessive hand-washing (three patients), and fear of being contaminated (two patients). Three patients had a history of depression. All six patients provided written informed consent. They were exposed to 10,000-lux white light for 30 minutes between 7:00 and 9:30 a.m. for 2 weeks. They were given the Yale-Brown Obsessive-Compulsive Scale, the NIMH Global Obsessive-Compulsive Rating Scale, and the 24-item Hamilton Rating Scale for Depression at weekly intervals by experienced raters.

RESULTS

The 34 subjects studied had a mean \pm SD global seasonality score of 5.4 \pm 3.7. A history of seasonal changes in mood and obsessive-compulsive symptoms of moderate to extreme degree was reported by 18 (53%) and seven (21%) of the patients, respectively. Twelve (35%) of the patients reported that seasonal changes had been a problem for them. Those patients who noted seasonal changes generally found that summer was the "best time" in terms of mood (12 patients) or obsessive-compulsive symptoms (five patients) and winter the "worst" in terms of mood (eight patients) or obsessive-compulsive symptoms (five patients).

The patients who received light therapy had a mean global seasonality score of 6.0 \pm 1.4. Of those light-treated patients who had noted a seasonal pattern in their obsessive-compulsive symptoms, two reported feeling "worst" in the winter and two in the summer. Their mean rating scores before and after 2 weeks of light therapy were as follows: Yale-Brown scale, 18 \pm 1.7 and 19.8 \pm 1.2; NIMH scale, 22.5 \pm 4.9 and 21.7 \pm 4.5; Hamilton depression scale, 14.2 \pm 5.2 and 13.8 \pm 3.9. These ratings were corroborated by subjective and clinical impressions that none of the patients appeared to improve substantially. There were no noteworthy side effects. All patients reported a higher number of vivid dreams during therapy, which subsided after treatment was discontinued.

DISCUSSION

As a group, the 34 patients with obsessive-compulsive disorder showed levels of overall seasonality com-

parable to those seen in the general population (9, 10). This finding does not contradict their frequent reports of marked seasonal mood changes, since this item contributes only a small degree to the global seasonality score. As in surveys of the general population, most patients with obsessive-compulsive disorder who reported seasonal variations found winter to be the most difficult time, both for mood and for obsessive-compulsive symptoms.

Light treatment did not prove helpful for the six patients with obsessive-compulsive disorder. Given the small and highly selected group of patients treated, the risk of a type II statistical error is high, and it would not be valid to generalize from this study to the potential value of light for all patients with obsessive-compulsive disorder. It is possible that duration and timing of treatment were not adequate to achieve a response.

Because a sizable proportion of patients with obsessive-compulsive disorder report marked seasonal variation in their symptoms, it might be worth exploring further the possibility that at least this subgroup might respond to treatment with bright environmental light. The evidence that brain serotonergic systems are dysregulated in both obsessive-compulsive disorder and seasonal affective disorder (11, 12) gives theoretical appeal to light treatment for obsessive-compulsive disorder. In view of our negative pilot study, however, we suggest that if clinicians or investigators wish to pursue this approach, they should start by selecting the most promising (seasonal) candidates and use longer exposures.

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New Policy for References

Effective with the September 1991 issue, *The American Journal of Psychiatry* instituted a policy of listing the names of all authors of work cited in references. Authors of submitted manuscripts and letters to the Editor must include the surnames and initials of all authors in references. The use of "et al." is no longer acceptable.

Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

The books for this month are a holiday gift list:
books to broaden the library and the mind,
to provide pleasure and enjoyment,
to give to oneself and others.

EDITORS' NOTE: We are indebted to Dr. Alan Stone for his imaginative suggestion that the Christmas issue of the Book Forum devote a part of its space to the psychiatric classics. That his idea has met with our enthusiastic response is evidenced in the three reviews that follow. We hope that Journal subscribers will take as much pleasure in reading them as the authors did in their writing.

N.C.A.
J.C.N.

L'automatisme psychologique, by Pierre Janet. Paris, Félix Alcan, 1889, 496 pp.

We wish, somewhat belatedly, to draw the attention of the *Journal's* readers to a remarkable volume published some 2 years ago, when its author had just reached the age of 30. Pierre Janet is not entirely unknown in modern scientific circles. During the greater part of the last decade he has served as professor of philosophy at the Lyceum in Le Havre, where, through the kindness of two local physicians, Drs. Gibert and Powilewicz (to whom the book is dedicated), he has been able to carry out extensive psychological observations on a small group of patients suffering from hysteria. The initial results of his studies have already been presented in several papers (1-3) in the *Revue philosophique*, with which readers may be familiar. The volume under review (which was submitted by the author as his doctoral thesis and earned him the degree of *doctorat en philosophie*) not only reproduces the essence of those studies but includes many additional observations and theoretical formulations that provide the reader with a masterful introductory treatise on clinical and experimental psychopathology.

In a short review one can hardly reiterate the details of a monograph that is nearly 500 pages long, and we shall limit ourselves to the barest summary of the author's methods, findings, and conclusions. Janet's approach to his research has been significantly influenced by the recent interest in experimental psychology, which, as evidenced by the writings of scholars like Taine (4) and Ribot (5), has drawn attention to the phenomena of psychopathology and their exploration by hypnosis. Janet's studies, as he tells us in his introductory chapter, have been guided by the scientific method of careful observation and systematic experimentation. It is Janet's genius to have recognized that the disturbances in sensation, volition, and memory that have been the focus of the work of others can best be examined and elucidated in hysterical patients, and it is to them he has turned as experimental subjects during his sojourn in Le Havre. It is further evidence of Janet's

creative vision that he has realized that the automatisms manifested as hysterical symptoms such as paralyses and anesthetics are accompanied by a circumscribed, elementary form of consciousness beneath the awareness of the patient's ordinary, more extended personal conscious awareness. Such automatisms are not, therefore, the result of merely mindless physiological processes (as has generally been taught) but are psychological in nature as well and can be appropriately studied by psychological procedures.

The importance of this psychological focus becomes readily apparent in Janet's examination of hysterical somnambulistic states. Here his observations reveal beneath the patient's ordinary consciousness a complex psychological structure of related memories and functions that constitutes a fully developed, secondary, self-conscious personality existing in its own right, distinct and separate from the patient's ordinary self. Moreover, this secondary personality, or "secondary self," co-exists with the primary personality and exercises a full range of psychological functions "unconsciously"—that is, it operates beneath ordinary consciousness without the conscious awareness of the primary personality. As a result of this "doubling" of the self, the underlying subconscious personality affects the functioning of the primary personality, producing automatisms in the form of sensorimotor symptoms and amnesia, whose source is unknown to the primary personality. Finally, to account for this doubling, Janet postulates a *misère psychologique*—a pathological lowering of psychological energy that compromises the individual's capacity to organize the totality of psychological functions into a single, unitary self and results in the *desagrégation* (the pathological splitting off or "dissociation") of constellations of psychological functions that compose the autonomous secondary personalities.

In making these observations and arriving at his conclusions, Janet has not been working in an intellectual vacuum. As we have noted earlier, his fundamental approach has been guided by the current principles of experimental psychology. But more than this, his omnivorous reading during his years in Le Havre has opened up to him the rich tapestry of the work and writings of others that reach back a century or more. Of particular note is Janet's familiarity with the extensive literature on magnetism dating to the time of Mesmer. This vast corpus of writings has until recently been ignored, if not held in total disrepute, and Janet's review has rescued from obscurity many facts known to his predecessors that, as Janet himself confesses, he is rediscovering in his own investigations. It was, indeed, only some 10 years ago that Charcot's important paper delivered to the Académie des Sciences (6) rehabilitated the study of magnetism under the label of "hypnotism," without which Janet might not have felt free to use hypnotic techniques as the basic tool of his experimental approach to hysterical phenomena.

It is clear, too, that beside his intellectual indebtedness to the recent writings of experimental psychologists in his own country, Janet has been considerably influenced by the publications concerning the little-known investigations carried out in England during the past decade under the auspices of the Society for Psychical Research, of which Janet became a corresponding member in 1886. He lists some 50 references to the annual proceedings of that organization and appears to be obligated to Gurney (7-9) for his important studies of post-hypnotic suggestion and to F.W.H. Myers (10) for the use of automatic writing as a particularly effective method for exploring subconscious processes.

Finally, we should note Janet's great familiarity with the literature of spiritualism, which has captured the imagination of the Western world since the first "spirit rappings" were reported by the Fox sisters in America over 40 years ago. More critical than many observers, Janet shows us how the phenomena of modern-day mediums, as well as the "devil possessions" of an earlier age, reflect the same mechanisms of dissociation that he finds in his hysterical patients. Lack of space prevents us from giving further testimony to Janet's versatile scholarship, but the copious references that dot almost every page of this volume will give the interested reader an idea of the range of readings and topics that have guided his observations and formulations.

We cannot close our review of this fascinating treatise without underscoring its most striking feature—the demonstration of the existence of unconscious mental processes. By employing the methods of experimental psychology, Janet has transformed into an object of scientific study the vague, romantic notions of the "unconscious" prevalent during the past century and so tediously elaborated in von Hartmann's tiresomely Teutonic text (11). In so doing Janet provides us with the basis for a new direction in the exploration of the pathology of mental disease, for he shows us that unconscious mental processes in the form of *idées fixes* underlie the production of clinical symptoms. The clinical study and care of patients with mental disorders must henceforth include attention to such unconscious factors.

Although Janet assigns a secondary importance to this aspect of his work, it is interesting to note that he is currently pursuing a medical degree in Paris while at the same time continuing his clinical investigations at the Salpêtrière under the aegis of Professor Charcot. One may hope that their medical applications will become the major focus of his studies in the years ahead. Whatever new findings he may uncover in his subsequent scientific research, we are already indebted to this volume for what is its single most important discovery concerning mental illness—that unconscious psychological processes are a central element in the genesis of clinical symptoms. As Janet himself has commented, his observations have shown the unconscious to be an empirically demonstrated fact, not a mere hypothetical concept. We may confidently expect that fact to play a vital role in the development of psychiatry in the century to come. It is a legacy that our psychiatric heirs will ignore at their peril.

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J.C.N.

(Editorial Postscript From "The Ghost of Christmas Yet to Come:" Late twentieth-century historians of the period treated in this review will be deeply indebted to Dr. Henri Ellenberger for his ground-breaking chapter on Pierre Janet in *The Discovery of the Unconscious* [New York, Basic Books, 1970], which will contain many of the biographical facts included here, and to the Pierre Janet Society in France for publishing a centennial edition of Janet's text in 1989.)

Dementia Praecox and Paraphrenia, by Professor Emil Kraepelin; translated by R. Mary Barclay, M.A., M.B.; edited by George M. Robertson, M.D., F.R.C.P.(Edin.). Edinburgh, E & S Livingstone, 1919, 328 pp.

Professor Emil Kraepelin has recently completed the eighth edition of his textbook, *Psychiatry*, which has been published in four volumes. Portions of this textbook have now been made more widely available to the English-speaking world through the recent translation of Dr. Barclay. *Dementia Praecox and Paraphrenia* translates a portion of volume 3, devoted to the endogenous dementias. Dr. Barclay has also translated other portions of volumes 3 and 4, in a volume titled *Manic Depressive Insanity and Paranoia*, which we will review in a later issue of the *Journal*. Dr. Barclay's translations may be especially helpful to American readers, who are often reluctant to become conversant in foreign tongues.

Professor Kraepelin has been director of the Psychiatric Clinic of Munich University for the past 17 years (since 1903). He is perhaps best known for his basic research in psychology, having received training in the experimental school of Wilhelm Wundt while completing his medical studies in Wurzburg. Professor Kraepelin will no doubt be long remembered for his work in the area of experimental and physiological psychology, having thoroughly delineated the effects of a variety of influences on the working curve and other aspects of intellectual performance. He has diligently investigated the effects of fatigue, a variety of poisons, and drugs such as tea, morphium, bromine, alcohol, and tobacco. He is internationally known for his leadership against the use of alcohol, having been a cofounder of the Society of Abstinent Doctors, lectured throughout Germany and in several other nations concerning the problems produced by alcohol consumption, and campaigned against the availability of alcohol to military troops during the recent war, a position perceived as somewhat unpatriotic by Bavarian beer merchants. Professor Kraepelin's work on the detrimental mental effects of alcohol should lend support to our own temperance movement here in America.

In addition to these salutary contributions, however, Professor Kraepelin's Herculean labor in producing textbooks of psychiatry should also be recognized. The eighth edition,

herein reviewed, represents a continuation of a long line of tomes that began with the publication of a *Compendium of Psychiatry*, the first edition of the textbook, written through the encouragement of Professor Wundt in order to assist Kraepelin in his teaching activities while he was serving as a University lecturer at Leipzig University.

Professor Kraepelin has based these textbooks on the somewhat unusual practice of systematically collecting large quantities of information over long periods of time. For many years, he has kept detailed case notes on all patients whom he has seen, followed them systematically in order to observe their outcome, and carefully documented the long-term course of their symptoms and functioning. In addition, he has traveled extensively in order to determine whether the manifestations of various morbid processes are the same in different countries throughout the world. The fruits of his travels to Java, India, Turkey, and a variety of other nations are manifest in this textbook.

Finally, he has extensively reviewed the writings of other colleagues. This textbook is replete with references to the work of other eminent scholars, such as Zendig, Deroubaix, and De Buck, as well as Professor Kraepelin's own colleagues from the Munich School, such as Nissl, Alzheimer, Brodmann, and Rudin. He is evenhanded in his allusions to the Swiss and Austrian Schools as well, repeatedly citing the work of Professor Bleuler and in general concurring with it. He does take exception to the psychology of complexes described by Sigmund Freud, who made a visit to America 10 years ago and has been favorably received in some circles since that time. Kraepelin's objection to Freud appears to be on the basis of method of observation rather than content: "As I am accustomed to walk on the sure foundation of direct experience, my Philistine conscience of natural science stumbles at every step on objections, considerations and doubts, over which the lightly soaring power of imagination of Freud's disciples carries them without difficulty" (p. 250). The text is marred only very infrequently by such partisan sniping, however, and is in general fair and scholarly in its review of contributions by others.

The portion of the textbook devoted to endogenous dementias makes a number of worthy contributions, of which American psychiatrists should become duly aware. Beginning with his seventh edition, Professor Kraepelin has proposed delineating the psychoses into a variety of subdivisions. Although he indicates that the boundaries between them may not always be clear, he has separated the endogenous dementias (of which dementia praecox is a prime example) from the endogenous mood disorders. Manic-depressive insanity is the major example of the latter class. This distinction is made largely on the basis of onset, course, and outcome rather than signs and symptoms. Typically, manic-depressive insanity does not lead to mental deterioration, while dementia praecox often does. Professor Kraepelin notes that there are exceptions to this general pattern. As has been pointed out by Professor Bleuler of Zurich, not all patients with dementia praecox experience deterioration of psychic functioning. In discussing genetic predisposition, Professor Kraepelin also notes that the boundaries between the conditions are not always sharp. For example, parents with manic-depressive insanity may produce offspring suffering from dementia praecox, although the familial pattern rarely occurs in reverse order (i.e., patients with dementia praecox rarely have offspring who suffer from manic-depressive insanity). As Professor Kraepelin notes, controversies about the defining features and boundaries of this endogenous psychosis are reflected in an ongoing controversy about how it should be named. Although Kraepelin's term "dementia

praecox" has been widely accepted, other possibilities have also been proposed, such as dysphrenia by Wolff, amblynoia by Evensen, paratonia progressiva by Bernstein, and schizophrenia by Bleuler. Because these other names are less comprehensively descriptive than dementia praecox, however, it seems unlikely that they will be adopted in its place.

In addition to its interesting conceptualization of the classification of endogenous dementias and psychoses, another major contribution of this textbook is its thorough description of the symptoms of dementia praecox. Professor Kraepelin's many years of taking careful notes and preserving documents provided to him by patients gives this book the richest description of the clinical manifestations of dementia praecox that has been presented to date. Many vivid examples are provided for various manifestations such as hallucinations, influences on thought, morbid tactile sensations, sexual sensations, disorders in the train of thought, manifestations of mental insufficiency, delusions, and disorders of judgment. In order to clarify and guide the student through these complex manifestations, Professor Kraepelin provides a balanced description of which manifestations are fundamental and which are less important. He embraces the distinction of Bleuler between fundamental disorders and accompanying phenomena: "The weakening of judgment, of mental activity and of creative ability, the dulling of emotional interest and the loss of energy, lastly, the loosening of the inner unity of the psychic life would have to be reckoned among the fundamental disorders of dementia praecox, while all the remaining morbid symptoms, especially hallucinations and delusions, but also the states of excitement, depression and stupor, further the manifold disorders of volition, negativism, automatic obedience, stereotypy, mannerisms, impulsive actions, would be regarded more as secondary accompanying phenomena" (p. 248).

Professor Kraepelin provides detailed statistics concerning the frequency of the disorder and its outcome. He also gives the student a thorough and highly scientific discussion of the causes of dementia praecox. Drawing on the research completed by his Munich colleagues, he devotes an entire chapter to the morbid anatomy of dementia praecox. Widespread disease has been noted in the nerve tissue, including swollen and sclerotic nerve cells and disarray in the order of cells within the various cortical layers. Professor Kraepelin notes that there may be two different groups of processes that account for these findings, one being morbid disorders caused directly by the disease and the second being losses occurring as a consequence of the disease. He notes that there is a probable relationship between the distribution of the morbid anatomy and the clinical picture of dementia praecox, although the specific details have not yet been demonstrated and are at present only hypothetical: "If it should be confirmed that the disease attacks by preference the frontal areas of the brain, the central convolutions and the temporal lobes, this distribution would in a certain measure agree with our present views about the site of the psychic mechanisms which are principally injured by the disease" (p. 219).

In addition to these various strengths, Professor Kraepelin's textbook does have some limitations. Perhaps most importantly, in its attention to detailed description, it sometimes ignores the psychic inner life. Professor Kraepelin shows little interest in inner subjective experiences and does not provide an adequate description of the psychic suffering of patients with dementia praecox. His discussion of familial aspects of the disorder is limited to the genetic sphere (with a comprehensive discussion of environmental influences such as toxins, infections, and birth injuries as well). He does not provide a full discussion of the psychological impact of this disease on

family members, nor does he discuss adequately the social and economic consequences of the disorder. The absence of this type of discussion is particularly striking, given his well-known advocacy of patient welfare and his attack on the use of restraints and other inhumane treatments in his own hospital. His somewhat hostile rejection of Freudian ideas appears to suffer from the same arbitrary dogmatism of which he accuses Freud.

Nevertheless, in providing this comprehensive survey of dementia praecox, Kraepelin has made a major contribution to the understanding of this particular form of insanity. As described by Dr. Robinson of Edinburgh in the introduction to this English edition, general paralysis of the insane has at last yielded up most of its secrets after a century of observation and research, leaving psychiatrists with dementia praecox as their remaining major disease, which produces an enormous toll in suffering and disability. The costs of this disease to its victims, their families, and society are enormous, since the disease often produces severe deterioration and causes its victims to require lifetime care. The availability of this excellent textbook should provide a major impetus to future research in dementia praecox. The nurturance of research in this disease in America, particularly if supported by assistance from state and federal governments, could build on the foundation that Professor Kraepelin has laid and ultimately yield an understanding of its causes, leading to improved treatment and perhaps even prevention.

N.C.A.

Three Essays on the Theory of Sexuality (1905), by Sigmund Freud, in *The Standard Edition of The Complete Psychological Works of Sigmund Freud*, vol. VII (1901–1905). Translated from the German under the general editorship of James Strachey in collaboration with Anna Freud assisted by Alix Strachey and Alan Tyson. London, Hogarth Press and the Institute of Psycho-Analysis, 1953

Infantile sexuality and repression are the twin cornerstones of Sigmund Freud's astonishing reconception of the human condition, and *Three Essays on the Theory of Sexuality* remains his most important work on those subjects. First published in 1905 as a text of 83 pages, *The Three Essays* had grown to 120 pages in the final edition in 1925, testifying to Freud's continuing interest in this book, which he considered the core of psychoanalysis around which everything else turned.

This book, first vilified and then accepted as dogma, changed the way the Western world thought about human sexuality. It is now almost totally neglected by psychiatrists. Like most of psychoanalysis, the basics have been assimilated into popular culture in bowdlerized versions and the fine points have become the subject of competing interpretations by narrow specialists. But a fresh reading of *The Three Essays* has a great deal to teach modern psychiatrists, even as we come to the end of the twentieth century.

The work is in some sense empirical, and yet Freud provides almost no evidence for his conclusions. The unspecified and perhaps unrecognized premise is that the author deals here with the universals of the human condition and that every reader, like Freud, has the necessary empirical evidence and need only be willing to reconsider his or her own experiences. Whatever its method, I know of no other work in psychiatry so powerful, so lucid, and so immediately convincing. The first two pages of the first essay, "The Sexual Aberrations," puncture

the conventional myth of sexuality: that the sexual instinct begins at puberty and is manifested by an irresistible attraction to the opposite sex leading to sexual union. Freud introduces two technical terms, the "sexual object" and the "sexual aim." With these as his conceptual tools he proceeds to deconstruct the sexual instinct and, in the process, illuminate sexual perversions, sexual foreplay, and sexual development.

He begins by discussing the psychiatric literature on sexual aberrations and particularly homosexuality. His point in selecting homosexuality is to emphasize the obvious deviations of the sexual instinct in respect to the sexual object.

Freud criticizes all of the medical explanations of homosexuality and specifically attacks the prevalent hypothesis that homosexuality is a form of mental degeneracy. His rejection of that hypothesis has a contemporary spin, employing arguments similar to those put forward when homosexuality was removed from psychiatry's diagnostic and statistical manual. Freud reasoned that if the concept of degeneracy is to have any coherent meaning it must exclude the possibility that in every other respect the degenerate nervous system is capable of efficient functioning. Freud always maintained that homosexuals could not be considered degenerate because among their number were persons of "specially high intellectual development and ethical culture," including "some of the most prominent men in all recorded history." Freud tentatively introduces his own theory that homosexuality is a developmental variant of a preexisting bisexual predisposition. In 1915 a confident Freud added the following footnote:

Psycho-analytic research is most decidedly opposed to any attempt at separating off homosexuals from the rest of mankind as a group of a special character It has found that all human beings are capable of making a homosexual object-choice and have in fact made one in their unconscious Thus from the point of view of psycho-analysis the exclusive sexual interest felt by men for women is also a problem that needs elucidating and is not a self-evident fact.

Freud's discussion of homosexuality is as enlightened and sensible as anything written on this subject in the twentieth century. It is unfortunate that gay psychiatrists have chosen to ignore this book and have made Freud a target of their criticism.

Freud goes on to discuss other sexual aberrations only to demonstrate how variable the object of the sexual instinct can be. He refuses to accept the standard convention that attributed sexual behavior which is socially or culturally horrifying to insanity. For example, he rightly observes that "the sexual abuse of children is found with uncanny frequency among school teachers and child attendants, simply because they have the best opportunity for it." This is a lesson from the first decade of this century that we still have difficulty accepting in the last decade.

Freud's intellectual audacity in this first essay accomplished something that has both psychiatric and moral significance. He looks to homosexuality in order to understand heterosexuality. In that process he begins the twentieth century's recategorization of homosexuality from degeneracy to developmental variation to sexual preference. In 1905, the analysis of homosexuality led Freud to the revolutionary hypothesis that "the sexual instinct is in the first instance independent of its object." Indeed, he concluded that the object is the most variable aspect of the sexual instinct.

His discussion of the "deviations in respect of the sexual

aim" establishes the relationship between foreplay and perversions, a connection that, once made, seems impossible to deny. It is a connection that in one move brings the outcast "perverts" back into the family of humanity and reveals the common structure of all the complicated dances of erotic life. These ideas unequivocally establish Freud's genius.

Unfortunately, Freud the genius reveals himself in these same passages as Freud the male chauvinist, who misunderstands female sexuality and belittles female character as "stunted" by civilization and "insincere." Most of his early patients were women, but Freud seems never to have gotten past his misconception that the female is in her essence as a sexual being a castrated and inadequate male. Freud's errors about female sexuality have been given many convoluted explanations. My own impression is that *The Three Essays*, like all of psychoanalysis, is ultimately grounded in Freud's self-analysis. His errors demonstrate the limitations of introspection just as his wisdom proves how much one man who knows himself can contribute to mankind. Freud knew more about men than he did about women, and that is obvious here in his most important work.

Despite this critical limitation, Freud's understanding of sexuality allowed him to see deeper into the human condition than anyone before him. He recognized that libidinalization leads to idealization and that the resulting overvaluation of the sexual object spreads to the intellect and influences judgment, so that the "credulity of love becomes . . . the source of *authority*." His sexual theory thus allows him to explain idealization, romantic love, and the psychology of the acceptance of authority. No serious intellectual in the twentieth century can ignore these ideas. He also identifies the dialectical oppositions in sexuality: active and passive, voyeurism and exhibitionism, and sadism and masochism. Moreover, he describes the naturally emerging repressive forces that act like dams on sexual development. Freud here explains why there is always such a close line between what is most sexually exciting and what is most disgusting. But the conceptual breakthrough of his "object" and "aims" analysis of the perversions is the conclusion that if the perversions have a "composite nature," then perhaps "the sexual instinct itself may be no simple thing."

Freud then turns his attention to his own clinical material on neurotics. He portrays these patients as having both "exaggerated sexual craving and excessive aversion to sexuality." He asserts that neurotic symptoms are based not only on conflicts about the "so-called *normal* sexual instinct" but also on conflict about what "would be described as *perverse*." It is in this connection that Freud claims that "*neuroses are, so to say, the negative of perversions*." This theoretical formula has been much discussed and criticized. Whatever etiological significance Freud's formula might or might not have, the basic point he intended to emphasize was that perverted impulses are not confined to pervers.

The grand theoretical leap integrating our understanding of perversions, neuroses, and the normal foreplay of sexual life was achieved by Freud's hypothesis that all are manifestations of some infantile component sexual instinct. Fixated, that component instinct is the origin of the perversion; repressed, it is the origin of the neurosis; integrated into normal sexual life, it is the origin of foreplay.

It is in his next essay, "Infantile Sexuality," that Freud turns from the pathological to the universal condition. His strategy is to begin with sexual aberrations and then to broaden the significance of his thesis by arguing that neurotics show evidence of perverse impulses. Now he extends his thesis to include all of humanity by describing the polymorphous, perverse sexuality of infancy. Freud was surely not the first person

to observe erotic behavior in infants, but no one before had made so much of it and its undeniable connection with adult sexuality in all of its variations.

Freud's intellectual master stroke was to introduce his other basic theoretical cornerstone—repression—to explain why others had been unable to recognize this obvious truth. This is the claim on which Freud built the whole edifice of psychoanalysis. The myth that children are as sexually innocent as angels is the result of infantile amnesia: we repress all of our own polymorphous sexuality and deny what we see in our children. The memories and the infantile experiences we repress are nonetheless what will determine "the whole of our later development." Infantile amnesia makes childhood like "a prehistoric epoch." We might assume that Freud could not have written this work without believing that he had overcome his own infantile amnesia.

Freud's ideas about repression would later be elaborated and reconceptualized. Here he makes a straightforward claim that repression is not simply a matter of education and cultural conditioning but that "disgust," "shame," and "the claims of aesthetic and moral ideals" are innate elements of repression. This development is organically determined and fixed by heredity. If there is a Freud the genius and a Freud the male chauvinist, there is also a Freud the eccentric. Most of his eccentric ideas center around his bizarre version of evolutionary sociobiology regarding the programming of human psychological development. For example, he posited that women discovered the weaving of clothing to conceal their lack of a penis and that men discovered fire by resisting the urge to urinate on it. Even in his greatest work there are speculations, characteristic of this great mind, that contain traces of those bizarre ideas.

Freud's familiar discussion of psychosexual development in the child charts out what has been called the "archeology of desire." The "blueprint" is interlaced with remarkably keen observations. For example, in discussing "the cruel component of the sexual instinct," Freud comments that cruelty "comes easily to the childish nature" because "a capacity for pity" develops later. Thus, he suggests there is a danger that the connection between the cruel and the erotogenic instincts will be unbreakable in later life. He warns about corporal punishment and its contribution to "the *passive* instinct of cruelty (masochism)." Read carefully, these passages contain an agenda for research in child development in the twentieth century that has never been completely achieved.

It is in a section on the sexual researches of childhood that Freud presents his theories of castration anxiety and penis envy and the importance of the link between sexual and intellectual curiosity. Many of these ideas have been criticized, and the concept of penis envy has been the subject of scorn, derision, and resentment of feminists. Whatever its failings as an explanatory concept, it is characteristic of Freud's tendency as a theoretician to portray psychological development in dramatic critical and transformative moments rather than gradual accretions. Penis envy, experienced in that supposedly revelatory moment of childhood, shapes the female character just as castration anxiety ushers in the harsh male superego. The very nature of the theory suggests a genius reflecting at a desk rather than an investigator observing child development.

In this same section, however, Freud in a few short paragraphs describes and explains the dilemma of love and marriage in the Western world. And like everything else in these essays it builds on what has come before. The child is a being of polymorphous, perverse, and autoerotic sexuality, and the primary love objects are the parents. The intense sensual current of the child's oedipal love of the parents must be repressed

and separated off from the affectionate current that remains in latency. Thereafter, sexual attraction has a tendency to be linked to the forbidden and the private, and affectionate love is linked to the permitted and public. Thus divided, the affectionate and sensual currents are difficult to bring together fully in a single love object. Much of what goes on in the psychodrama of modern marriage and infidelity is still best understood by reading Freud.

Freud's final essay is entitled "The Transformations of Puberty." Having so thoroughly deconstructed sex by his convincing descriptions of the variations of sexual object and sexual aim in perverts, neurotics, and children, even Freud is hard pressed to put it all back together. Everything that was a mystery has been explained, but now what was obvious—the attraction between the sexes—has become a mystery. Freud does no more than impose on the component instincts a normative hierarchical coherence. All of the zones, aims, and objects that come before are to be assimilated under genital primacy and subordinated to the reproductive function in heterosexual object choice. It is in this section that Freud's fateful discussion of clitoral and vaginal sexuality occurs. Looking back from the vantage point of the end of the twentieth century, one can only imagine how many women's self-confidence in their sexuality was undermined by Freud's pronouncement. Vaginal orgasm as the ultimate expression of female sexuality was accepted as dogma and presented to educated women as the norm by which their psychosexual maturity was to be judged. Therapy for sexual dysfunction has been one of the notable achievements of modern psychiatry, but Freud's ideas were an impediment to the development of effective treatments for women.

I have read, reread, and taught *The Three Essays* for four decades. During most of that time I tried to distinguish which parts of the work revealed Freud's genius and which parts revealed his eccentricity. Although I still believe the distinction can be made, I am now convinced that Freud's eccentric ideas are not momentary lapses but structures in the intellectual edifice his genius has created. Despite its flaws, Freud's paradigm of the human condition has dominated the twentieth century, and *The Three Essays* offers the reader the most intriguing encounter with the mind that created psychoanalysis.

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LITERATURE

Darkness Visible: A Memoir of Madness, by William Styron.
New York, Random House, 1990, 84 pp., \$15.95.

Patients can present psychiatrists with an astonishing parade of chief complaints—even veteran psychiatrists are awed at times by the Byzantine complexities they are called upon to unravel—but, without question, "depression" is one of the most commonly proffered difficulties. Depression seems like a straightforward complaint, until one seeks precisely to map the wide landscape cloaked by this simple word, which in the realm of clinical medicine is both a symptom and a diagnosis. The clinical term appears multifariously throughout *DSM-III-R* (e.g., major depression, dysthymia, depressive neurosis, adjustment disorder with depressed mood, etc.), and the usual patient applies this word to feelings ranging from simple unhappiness or sadness to imprisoning melancholia. It is, nonetheless, difficult for one word to express the fullest implica-

tions of dysphoria, and when it comes to describing depression's blackest hole, mundane language is a bit thin.

Pulitzer Prize-winning author William Styron calls depression "a wimp of a word for such a major illness." As a man who has suffered this affliction and, in his words, returned to tell the tale, Styron prefers the expression "brainstorm." After agonizing within the storm of major depression throughout the late summer and autumn of 1985, the man whose talent created *The Confessions of Nat Turner* (1) and *Sophie's Choice* (2), among others (3, 4), was existentially lost and near suicide. Having concluded that no more words need be written and that silence was elegantly more preferable than a suicide note, Styron sat alone one cold December night, unable to sleep, accompanied by the beckoning remembrance and promise of Brahms's *Alto Rhapsody*. In the pit of desperation, Styron recalls that he "drew upon some gleam of sanity," and the following day, at his own behest, he was admitted to the psychiatric inpatient service at Yale-New Haven Hospital.

Darkness Visible is a compelling personal narration of Styron's travels to the boundary of madness and of his eventual return. It should be requisite in the core curriculum for psychiatric residents and is highly recommended reading for clinical psychiatrists. The book is quite short, an extension, in effect, of a monologue presented by Styron to the symposium on affective disorders sponsored by the Department of Psychiatry of Johns Hopkins University School of Medicine in May 1989.

The narration commences with a trip to Paris in the autumn of 1985, when Styron was to receive a prestigious literary award. Revisiting the site of his early career, he found himself prepossessed and loathe to attend a luncheon in his honor, ungraciously offending his benefactress. This atypical behavior was a pivotal manifestation of the menace that was devouring him, and Styron began to comprehend the clasp of "un problème psychiatrique" that had begun many months earlier when he underwent a forced abstinence from alcohol. Even though he adamantly maintains that he never wrote under the influence, he freely and unapologetically admits to abusing alcohol throughout adulthood as a soothing bridge to creativity. Then, suddenly, his body betrayed him by generating a disulfiram-like reaction. Feeling as if abandoned by an old friend, Styron reluctantly accepted the forced abstinence. The changes that followed were initially subtle, almost imperceptible, but eventually vulnerabilities became a major focal point for him, and by the autumn Styron was entombed in a neurovegetative outland. His mood had turned unrelentingly dark, and the difficulty had become all too visible. In one revealing scene he tells of a magazine editor who diplomatically requested a second photo session because the results from the initial sitting were rejected as "too full of anguish."

The emphasis of the book is on the darkened journey through the development and clinical course of major depression with melancholia, not the resultant hospitalization and therapy. Styron willingly acknowledges his need for hospitalization, but the best he can say for group therapy is that it is "a way to occupy the hours," and he disparages art therapy as "organized infantilism." Styron remained hospitalized for nearly 7 weeks and eventually exited the storm, discovering that, beyond scientific medicine, the most effective healers were time, sanctuary, and the fellowship of friends.

William Styron is by no means the first writer to become alcoholic, depressed, or suicidal. Writing, by its core nature, can be a lonely, self-reflective pursuit, and Styron's story is replete with poignant vignettes of literary and creative acquaintances who have also suffered the painful weight of mental illness. In *Alcohol and the Writer* (5), Donald Goodwin

explored the epidemic of alcoholism among famous American writers. The revealing biographical sketches in this study make it an excellent companion volume. As with other eminent authors (6), Styron's price tag for the "creative leap" may well be a soul-stirring susceptibility to melancholia. But he now knows the brainstorm can be conquered.

The last page of *Darkness Visible* is a short autobiographical footnote highlighting the author's literary accomplishments. It cites Styron's service in the United States Marine Corps during World War II and the Korean conflict—a seminal experience that defies repression and has collaborated in the forging of his self-concept and tempered his writings. According to the postscript, William Styron is currently finding faith in remembrance of things past and writing a long-contemplated novel with the Marine Corps as a central setting.

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Lying Together, by D.M. Thomas. New York, Viking, 1990, 247 pp., \$17.95; \$8.95 (paper).

The idea that life resides in imagination and art is the vivid theme of D.M. Thomas' *Lying Together*, the fifth in his quintet of novels, *Russian Nights*. Thomas makes his point with puns, send-ups of politically correct, cliché-ridden intellectuals, and startling fantasies, deftly transmuted into realities that slide imperceptibly into other, unexpected forms. The story is set at a writer's conference in a London hotel that gets mixed up with a funeral director's convention, featuring, among other events, a solemn speech on "The Preservation of a Cadaver," which is greeted with respectful references to Borges by the lively, obstreperous literary types and with rapt interest by the dull-as-dust undertakers.

The author, Don Thomas, here a character in his own novel, meets his three Russian friends, novelists with whom he collaborated at other meetings in marathon improvisations that resulted in the earlier volumes of the *Russian Nights* series—or did they really? Late at night, the four begin again, playing out their own complicated relationships in the improvised story that takes unexpected turns of motivation and plot. Who is lying? Who is lying with whom? And which combinations of real and fictional characters are lying together? Dreams and literary fantasies are sewn into a patchwork narrative: Krafft-Ebing's real or imagined correspondence with a housemaid who is shocked and titillated by his work; a star turn in which Freud, painfully ill with cancer, describes in German, through the mouth of one of the improvisers, his childhood dreams; rapturous bisexual moments shadowed unexpectedly by the specter of AIDS; and repetitive dreams about terrifying climbs up and down the ice-slick Eiger North Face, the "Wall of Death." One of the Russians, more madcap than the others,

tells, deadpan, about his sexual experiences with Margaret Thatcher—"[she] is still tingling from our session together. But what can I do? There's no future for us."

With improvisation at an end, and the embryo of *Lying Together* temporarily entombed in his tape recorder, to be resurrected later, Thomas returns home to Cornwall. On the train, he sits opposite a young, pregnant, red-haired woman. Her eyes, "zloi, cunning, knowing," give her away as Avav-nuk, the Eskimo spirit-wife and muse of Rozanov, one of the *improvisatore*. Asked about her violence as a lover, and about death, Avav-nuk explains, "Death is life's lover. They lie together." And indeed they do, certainly in this choice exercise in literary cunning, and perhaps in all of our lives.

Think about it.

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Selected Poems of Vern Rutsala. Santa Cruz, Calif., Story Line Press, 1991, 300 pp., \$21.95; \$16.95.

Poetry may be the form of verbal expression least amenable to brief review. Poetry requires the concentration of ideoaffective complexes into tiny phrases that explode into associative splendor when taken into the core of an accepting reader. Book reviews require condensation of extensively elaborated themes and ideas in such a way that their reader may decide whether to invest time and energy in a book, to add water and undo the dehydration of a review. I wish to convince you that something about Vern Rutsala's poetic vision resonates with your own clinical vision, that he speaks for some part of you.

Knowing of my interest in the emotion shame, more than a dozen people from all over the country sent me photocopies of Rutsala's poem "Shame" when it appeared in *The American Scholar* (1). A deeply moving description of shame as it is lived, the poem impelled me to investigate further the author and his work. *Selected Poems*, his recently released collection, traces the work of this gifted poet over a 30-year period.

Technical aspects, for those who care about such things: Rutsala's poetry tends to be written in a radial style—each line interacts both with its predecessor and its successor, often in so startling or "disturbing" a manner that one is forced to read a passage several times because it appears to change direction so dramatically. Radial, too, because our associations move us laterally just as the poet moves us up and down his page. This is a poet who means to distract us by causing maximum interaction with our inner life. Rutsala's imagery is the essence of crisply honed primary process in art—things become scenes become eras become affects become us rather than him while leaving us always aware of the poet who took us there.

Rutsala stands aside from what he views, much as the experienced clinician adopts a hovering stance midway between self and other. Getting to know him, we come to realize that the distance he chooses is directly proportional to the intensity of affect contained in the scene evoked; often it is the distance itself that warns us we are soon to be overwhelmed by whatever has forced him to write the poem. This American of Finnish extraction who labored with his father to build houses in the arid cold of Idaho, who knew the stultifying chill of poverty and the warming blur of booze, who sees history in junkyards and time travel in trains, this man whose life and vision is so skew to my own, speaks for a part of me I never knew.

Often, reading Rutsala, I am reminded of a short story by Ray Bradbury in which an American explorer sits on a Martian hillside watching a real and current vehicle travel toward

and through the ghostly image of one from Mars of ancient days which moved on that same road in the opposite direction, the inevitable crash silent and harmless because the vehicles were separated by millennia. These poems make my head spin. They force me to think.

Images, lines, phrases that affected me: "On the playground/patient children/are learning how/to break the rules/day by day. I see/the cheat, quick hands/making ready for a future of short/change; the liar/practices his surgery on the real; and the fool/wears his freckles/like a mask, buck-teeth/grinning at the beautiful" (pp. 19–20). On taking over a house formerly occupied by others, he notes, "Wallpaper/has memorized/the places where/their pictures hung" (p. 29). Noting that our associations to words themselves can be daunting, he asks, "What words will carry terror/in a place where the typewriter/weights heavy with demands/like a medal made of a millstone?" (p. 40). On the tendency of memories to distract: "I stroll along the staggering sidewalk/and from here, this dated day, this window/the broken rudder of my mind/drifts among the noises of the street/that is the debris of another, future evening" (p. 44).

He remarks on the disparity between financial poverty and the wealth of words available to him: "We had more than/we could use./They embarrassed us,/our talk fuller than our/rooms. They named/nothing we could see—/dining room, study,/mantel piece/lobster/thermidor. They named/things you only/saw in movies" (p. 151). On the welcome disavowal of the barroom: "And this is why/we come here now, why we lose/to bar dice, to liar's poker/and the slaughterhouse cries of songs./We have companions here—the people/we used to be" (p. 234).

Near the end of this superb collection Rutsala comments on the painful craft of poetry, reminding us, "And so poets/drink or otherwise kill/time that's out to make them/flop helpless in their own/dust. At heart they're accountants/and scholars of sound,/but they flop around and get/in trouble by insulting/the right people, rolling their/eyes like pinball machines" (p. 272).

It is vision like this that made me leave the comfortable practice of endocrinology and take up the study of the unconscious. I suspect you, too, will find here much that rewards your own struggle to face what is daunting in the inner life that both links and separates humankind.

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Possession: A Romance, by A.S. Byatt. New York, Random House, 1990, 560 pp., \$22.95; \$12.00 (paper).

This is a wonderful book. It is one of those old-fashioned, big, fat books we used to read. It has a heroine, Maud, and a hero, Roland, two young academics in English literature, who come to believe that the Victorian poets in whom they are each interested may have known each other. *Possession* is, among poetry, letters, diaries, and romance, the detective story of their quest to learn about this relationship. Of course, the poets did know each other both professionally and romantically, or there would be no story.

But what makes the book so fascinating is that it is an interweaving of two quite different stories. One of the stories is a postmodern and feminist account of the two young academ-

ics, and the other is a Victorian novel about the poets replete with their poems, letters, and diaries. The language and style of each of the two stories are appropriate to its time, and the reader has the adventure of going back and forth between them. Thus, it seemed daunting to me to face, on page 173, 47 pages of letters, but, gradually, as the passionate Victorian courtship carried out in the correspondence evolved, I became fascinated at both its progression and the author's skill in depicting it. On the other hand, I must admit to skipping some of the poetry while enjoying the humor (perhaps unintended?)—a "conference on sexuality and textuality" and a paper titled "Melusina and the Daemonic Double: Good Mother, Bad Serpent."

But what is most interesting about *Possession* is the contrast between two sensibilities, modes of experiencing the world, or discourses—the Victorian and the postmodern. Maud, who runs a woman's resource center, states the problem, "We live in the truth of what Freud discovered Once they [the Victorians] knew God valued them. Then they began to think there was no God, only blind forces. So they valued themselves, they loved themselves, and attended to their natures" (p. 277). Later, Roland continues, "We never say the word 'Love,' do we—we know it's a suspect ideological construct—especially Romantic Love—so we have to make a real effort of imagination to know what it felt like to be them, believing in these things—Love—themselves—that they mattered" (p. 290).

The Victorian couple do not analyze their love; rather, they possess it, or it possesses them. She says, "But now, my love we are here, we are now, and those other times are running elsewhere." He says, "You are safe with me," and she replies, "I am not at all safe with you. But have no desire to be elsewhere." The narrator, while speaking of the modern couple, notes, "Things had changed between them nevertheless. They were children of a time and culture that mistrusted love, 'in love,' romantic love, romance in toto and which nevertheless in revenge proliferated sexual language, linguistic sexuality, analysis, dissection, deconstruction, exposure. They were theoretically knowing: they knew about phallocracy and penisneid, punctuation, puncturing and penetration." They do not know about love, but in the course of the book they learn, in large measure from the Victorian poets.

We may believe that our current knowledge encompasses what has preceded it, that it is superior to past ways of thinking, and even that we can have access to previous modes of being and understanding. But this is clearly mistaken, for better and for worse. Today, we cannot not analyze. As a young man in a cartoon says to his girlfriend, "But Sarah, analyzing our relationship is the basis of our relationship." The ego and ego analysis have been replaced by relationships and family therapy.

Postmodernism emphasizes the multiplicity of discourse, the power relations that govern which will prevail, and the lack of a secure center. We see our predicament in everyday life, where the reactions in the press to a *Vanity Fair* photo cover of a nude, very pregnant Demi Moore or to the movie *Thelma and Louise* make us realize how many modes of experiencing life coexist today. Feminists cannot agree whether Moore is being exploited or whether Thelma and Louise "are poor role models."

How we construct and deconstruct our feelings, whether in psychoanalytic or biochemical discourse (in *Ninotchka*, Greta Garbo says, "Love is just chemistry"), will influence how we experience these feelings and how we live. Havens (1), in his description of the "schools," and McHugh and Slavney (2), in their account of the "perspectives," point out the very dif-

ferent and incompatible visions of man that exist in psychiatry today. Interestingly, Havens believes that one should specialize in a school in order to maintain focus, but McHugh and Slavney think that one must attempt to encompass all of the perspectives or risk overlooking vital aspects of a patient's life.

The real adventure in *Possession* is the encounter between our postmodern selves and other possible selves that some of us may have known, possibly in the persons of our grandparents. The special bond between grandchildren and grandparents is well-known. We are now far enough from the Victorians not merely to decry aspects of their beliefs and modes of being but also to envy them.

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MUSIC AND ART

Psychoanalytic Explorations in Music, edited by Stuart Feder, Richard L. Karmel, and George H. Pollock. Madison, Conn., International Universities Press, 1990, 526 pp., \$60.00.

The difficulty in writing sensibly about music is, comparable, perhaps, to the difficulty we experience trying to translate feelings into words, to objectify the ineffable, to express the inexpressible. Musicologists and critics have generally resorted either to factual biography and/or examination of historical context, to analog interpretation, or to strict musical analysis. Feder, Karmel, and Pollock provide us with 22 papers from the last 40 years that attempt to apply psychoanalytic understanding to the problems of music: the mind of the creator, the creative act, the meaning of the product, and its effect on the listener.

The first of the book's four sections deals with contributions to the psychology of music: What is the musical experience? What does music mean? After early contributions of id psychology and topographic theory we move on to the ego and structural theory, with attendant concern with adaptation, cognitive style, and mastery. Section two examines the origins of musical ability, musical endowments, and their development. A number of the papers echo Greenacre's postulation of special sensory givens and early reinforcement, perhaps particularly maternal. The third section attempts to explicate the process of creation, the shaping of the passage of sound and silence through time into musical structure. As Nass points out, we cannot simply translate music into verbal meanings: "Nondiscursive materials need to be understood in their own terms. The attempt to translate them into discursive modes often results in both losing their meaning." Nonetheless, a number of the authors suggest the importance of dealing with loss and mourning, an "aesthetic crystallization of . . . nostalgia." Or, again in the words of Nass, "the talented individual is able to experience and reexperience early separation trauma and face new material with courage and imagination. This capacity involves an ability to remain open to developmentally earlier modes of thought and rather than being conceptualized as regressive requires a greater degree of ego strength for its implementation."

The fourth and final section examines the lives of individual

composers, from Mozart to Ives, using the techniques of applied psychoanalysis. The usual caveats apply: we are missing the individual's associations and through them the opportunity to correct our mistakes; we must not mistake the product for the person. These papers are written by some of the most sophisticated and careful workers in the field: Esman, Ostwald, and Feder. Maynard Solomon offers a rare view of other aspects of Mozart's genius in his paper on Mozart's Zoroastrian riddles.

All in all, despite some dated but still historically interesting papers, this book, monograph 3 in International Universities Press's Applied Psychoanalysis Series, provides a positive cornucopia of riches. In an afterword the editors state that they have attempted to establish a field of interdisciplinary inquiry. I hope that further volumes in this series are planned.

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Psychoanalytic Perspectives on Art, vol. 3, edited by Mary Mathews Gedo. Hillsdale, N.J., Analytic Press (Lawrence Erlbaum Associates, distributor), 1988, 314 pp., \$39.95.

This book is an engaging collection of essays that examine art from a psychoanalytic viewpoint. It is composed of four sections. The first three consist of 17 essays that focus on art and artists from different historical periods—Renaissance, surrealist, and modern. The last section contains two book reviews of James Lord's controversial biography of Giacometti. The authors of the essays include scholars from many disciplines, including psychoanalysis and art history.

In the Renaissance section, John A. Phillips employs a unique combination of artistic, historical, and theological analyses in his compelling exegesis of Michelangelo's depiction of Eve in the Sistine Chapel. He asserts that "The Creation of Eve" is placed centrally on the ceiling's vault between "The Creation of Adam" and "The Temptation and Expulsion" because Eve is central to Michelangelo's theological conception. Phillips then explains that Eve's gesture to her genitals in "The Temptation and Expulsion" is meant to suggest the nature of the original sin, as well as to foreshadow the Second Eve, who will bring redemption through the virgin birth of the Second Adam.

In the surrealist section, the longest in the book, the effects of early childhood trauma on the art of both Giorgio de Chirico and Max Ernst are discussed. Both of these artists suffered profound losses as youngsters. De Chirico lost his older sister when he was 3 years old and his father when he was 16. Nancy Scott discusses De Chirico's depiction of his father as idealized yet aloof: the omnipresent frocked statue in his series of metaphysical paintings. This essay succeeds in skillfully linking De Chirico's iconography in the *Pittura Metafisica* with the themes of departure and return, abandonment and reconciliation, and the recurrent imagery of his father and fatherland. In the *Return of the Prodigal*, works executed in 1917–1919, De Chirico depicted himself as a mannequin, returning to the embrace of his father with his nineteenth-century values. These pictures brought to an end De Chirico's most inventive works. Whereas Scott is concerned with illuminating the sources of the statues depicted in the paintings and describing the artist's feelings toward his homeland, Milly Heyd—relying on De Chirico's early memories—offers a more thorough psychoanalytic discussion of his sibling rivalry and oedipal guilt. Heyd's analysis of De Chirico's unresolved feelings toward his older sister is better

developed and more convincing than her discussion of his enmeshed relationship with his brother.

In the two essays on Max Ernst, art historian Charlotte Stokes and psychoanalyst Leon E.A. Berman collaborate to elucidate the personal meaning of Ernst's imagery. Stokes demonstrates how Ernst used his knowledge of Freud to develop his free-associative technique. In addition, she relies on specific biographical data to show that Ernst's famous bird imagery is closely associated with his relationships and identification with his sisters—the four surviving ones as well as the two who died during his childhood. While acknowledging that primal scene memories were by no means the sole driving force in Ernst's work, Berman interprets passages from Ernst's autobiography to explain the role of such fantasies in his art. Also in this section, Donald Kuspit offers a more theoretical piece on what psychoanalysis can learn from surrealism: to dare to take a more revolutionary stance in truly changing society by going beyond the "miserabilism" of common sense to embrace the sense of the "marvelous" offered by the irrational, imaginative mind.

In the section on modern art, Mihaly Csikszentmihalyi insightfully discusses the fine line between the art of the mentally ill and that of modern artists. He first presents data from empirical research demonstrating that young art students are more reserved, less bound by social norms, and more imaginative than average students. The danger facing those who break away from shared norms, he warns, is slipping exclusively into their inner worlds. He writes, "In the past, pain and fear could be credibly transformed through a symbolic vocabulary that gave meaning to suffering." But the "modern artist has no access to symbols that will alleviate existential pain . . . and when he reaches into the psyche without transforming cultural symbols, what he finds there are the same nightmares that haunt the insane."

Whereas the essays in the surrealist section sometimes become a bit heavy-handed in their application of psychoanalytic theory, both Catherine C. Bock's essay on Matisse's self-portraits and K. Porter Aichele's on the Vienna School are refreshing in that they rely more exclusively on biographical data and, in Bock's case, a developmental approach, to explain the personal nature of these art works. Bock tells of the different ways in which Matisse chose to represent himself in images: through introspective self-portrait paintings in the early stages of his career when he was groping for an artistic identity, and through professional photographs as a mature artist when he sought to present himself as the vision of bourgeois respectability. Interestingly, in his later years, facing a life-threatening illness, Matisse returned to the self-scrutiny of his youth to draw self-portraits, after a break of 20 years.

Although it is well-known that after World War II the New York School artists were using surrealist and psychoanalytic techniques to plumb unconscious depths, Aichele's essay shows how these techniques were also used by painters of the Vienna School. Although the New York School renounced all past realistic styles, the Viennese painters transformed the traditional techniques and religious iconography of Northern Renaissance masters into powerfully personal artistic statements.

The final section of this volume consists of two reviews of the book *Giacometti: A Biography* by James Lord. While acknowledging the comprehensiveness of Lord's research, both Frank Galuszka and Laurie Wilson comment on the detrimental effects of Lord's overidealization of and overidentification with the subject of his study.

At the end of this volume, one is left with a deeper appreciation of the ability of psychoanalytic interpretation to eluci-

date the personalities and conflicts of artists as revealed in their work. At the same time, however, one is continually struck by the fact that the artwork itself transcends such interpretation—no matter how ingenious in its complexity. Whereas Freud was a master at bringing clarity to chaos, a Kuspit provocatively puts it, "Freud's dismissal of art as illusion . . . ignores art's power to rejuvenate life by romanticizing it. Where common sense deadens, art's uncommon sense revitalizes."

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Hugo Wolf: Letters to Melanie Köchert, edited by Franz Grasseberger; English edition and translation by Louise McClellan Urban. New York, Schirmer Books (Macmillan), 1991, 279 pp., \$29.95.

Hugo Wolf appears to fit our very image of the Romantic composer. Born in 1860, his early life was turbulent. Chronically in difficulty with authority, he was thrown out of a series of schools. He was appreciated for his musical skills, however his father was a gifted self-taught amateur musician and Hugo's first music teacher. Hugo's difficulties continued in the Vienna Conservatory: he was dismissed for "breach of discipline." He struggled to support himself by teaching and for acceptance of his music, mostly without success. He lived in garrets, slept on the floor at friends' homes, and remained dependent, despite his problems with authority, on the good will of a number of patrons. Among these patrons were the Köcherts (and Josef Breuer).

Heinrich Köchert was a prominent Viennese court jeweler; his wife, Melanie, was Wolf's devoted friend (and probably more) for 24 years. This book, along with introductions and notes, provides us with the extant correspondence between them: 245 letters written between 1887 and 1899. Unfortunately, her letters are lost, and she destroyed the more intimate of his. There is also the rare deletion, where she would cut a sentence or more before leaving the letter to posterity. In their entirety, the letters detail the ordinary vicissitudes of an extraordinary life as Wolf makes his way from city to city and from friend to friend, unsuccessfully peddling his music to publishers and performers. Meanwhile, he writes to request that his winter coat be sent on to him, or complains that the new shirts have arrived but don't fit properly, or would Melanie please see that his new electric cigarette lighter is fixed. He also outlines his continuing difficulties in getting his music performed: a singer cancels, a concert is postponed, the singer or the orchestra or the conductor is poorly prepared. He describes the difficulty of travel, his accommodations, the weather and scenery, the books he is reading. About a volume of poetry, for instance, he writes, "A boring whine of hear and hurt, loving and shoving, moaning and groaning, yearning and burning and whatever other trash can be drawn from the lyric junk room." Over the years the letters get longer, drop "best regards" to her husband, and hint at more intimacies.

The most remarkable feature of Wolf's communications however, is their consistent sanity. Letters, after all, only parallel a life; during this period Wolf continued to suffer from repeated depressions that interfered with work but were punctuated with unpredictable and often intense bursts of creativity. At the least, Wolf suffered from cyclothymia and perhaps from manic-depressive disorder. (His father was described as moody and introspective.) He also became ill with syphilis

presumably in 1877, and in 1896 was noted to have Argyll-Robertson pupils. Wolf's last letter to Melanie is unsigned, written in 1899 from the asylum where he died from tertiary syphilis 4 years later, requests a suit, shoes, and a new overcoat. He adds, "Whether I'll be permitted to leave the asylum is still very doubtful, however, or actually not doubtful, because how am I to get out of here without help from my friends?" Melanie Köchert did not desert Wolf as he slipped into demented madness. She visited him three times a week until his death. Three years later she fell to her death from the window of her home in Vienna.

Unfortunately, no recent biography of Wolf exists in English; there is merely a long biographical note by Eric Sams in the *New Grove Dictionary of Music and Musicians* (1). Just as the letters parallel his life, this volume would most appropriately act as a supplement to a biography. Nonetheless, if one bothers to listen between the lines, it will deepen one's appreciation for the music of one of the masters of German song.

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BIOGRAPHY

Vaslav Nijinsky: *A Leap Into Madness*, by Peter Ostwald. New York, Lyle Stewart (Carol Publishing Group), 1991, 358 pp., \$19.95.

Ever since I was a college student a great many years ago, photographs of two ballet scenes have adorned the walls of my home. One of these is of Nijinsky shaping his body into a perfect cross in his unforgettable and favorite role of Petrushka. There has been a never-ending stream of books on Nijinsky, an unfathomable genius who defies the ordinary categories of psychiatry, as does any individual of such extraordinary talent. Psychiatrists have been attempting to "analyze" Nijinsky from almost the beginning of psychoanalysis. For example, in 1981 an excerpt from Alfred Adler's previously unprinted preface to Nijinsky's diaries was published (1), in which Adler in 1936 presented a theory of schizophrenia using Nijinsky as a case study. Ansbacher (2) reported that out of consideration for Nijinsky's wife, Romola, Adler had to leave out an important aspect of his theory, dealing with her role in her husband's disorder. Indeed, the first books I obtained on Nijinsky many years ago were by or edited by his wife (3-5) and present an extremely biased and unreliable view.

Since a number of standard and popular biographies of Nijinsky have appeared after his wife's propaganda, it is reasonable to ask what justifies yet another book about this remarkable genius. Nijinsky's sister (6) published her memoirs of their early life. Krasovskaya (7) wrote a beautiful biography, the first in Russian, which was published in Leningrad in 1974 and translated into English in 1979 with some outstanding pictures. Krasovskaya admirably accomplished her aim "to tell the story of the tragic fate of an artist who expressed the abrupt disjunctions of his age and who, in many ways, antici-

pated the later paths of development in twentieth-century ballet." She also attained her second goal in this book, "to apprehend—within Nijinsky's fateful life—certain general characteristics of the psychology of artistic creativity, links between the artist and his time, and ways in which a historical period conditions artistic personality" (pp. v-vi). I doubt if it adds to our knowledge and understanding and appreciation of Nijinsky to be told in the appendix to the book under review here that his diagnosis according to *DSM-III* "must be Schizoaffective Disorder in a Narcissistic Personality" (p. 350), but Ostwald's main text does have a genuine contribution to offer.

Although Ostwald's book contains some nice photographs, these have been chosen more for their biographical interest than to portray Nijinsky's incredible sensitivity and capacity to make every facet of his body yield to whatever he wished to create at any given time—a capacity that defies description in ordinary language and certainly transcends our simplistic *DSM-III-R* diagnostic categories. Ostwald, Professor of Psychiatry at the University of California in San Francisco, documents quite well the dark side of Nijinsky. This baffled such famous Continental clinicians as Eugen Bleuler, Ludwig Binswanger, and Manfred Sakel, when, in his 30s, Nijinsky became disturbed and then grew progressively more disabled in his 40s and 50s. As the profession of psychiatry has learned, one hopes, in the case of Ezra Pound, the development of a psychosis in a truly creative genius is so complex and so difficult to separate from its creative aspects that one pales at undertaking to describe such phenomena using our ordinary clinical terminology.

Nijinsky died in 1950 at the age of 61 in London. Ostwald's preface tells us that, appropriately for a psychiatrist, he intends to focus on the last 30 years of Nijinsky's life, when he was increasingly pathological. To get Nijinsky's children to cooperate, Ostwald tells us he had to agree "to show the Nijinskys all my findings and to publish nothing of which they disapproved" (p. xi). A great many doctors and hospitals from various centers all over the world also cooperated, providing Ostwald access to many records that enabled him to document Nijinsky's developing illness and myriad treatments. This makes Ostwald's book a worthwhile endeavor and a sincere effort. There was a childhood injury that may or may not have affected Nijinsky's brain: "Clearly there had been severe trauma, both physical and psychological" (p. 12). Ostwald is understandably vague as to what extent this "accident" affected Nijinsky's performance and his life, and I do not know how it could ever be determined. This is one of the biggest problems of psychohistory—trying to examine psychiatrically or to psychoanalyze someone who is no longer alive and cannot be interviewed or studied directly.

Nijinsky's life-long search for love and his tendency to depression led him to be exploited by a variety of individuals; these are well documented by Ostwald, but there is little explanation of his homosexuality. Ostwald tells us he was bisexual (p. 31). At times he is uncritical; for example, we are told, "Nijinsky's penis, at least in its nonerect state, was said, by his sister, to have been under size (she may have been remembering him as a child)" (p. 20). Ostwald writes his book for the general public, in a popular reportorial style. This is not a technical book for professional historians, but I would have no hesitation in recommending it to psychiatrists as light vacation reading. I would suggest that the texts by Krasovskaya (7) and by Nijinsky's personal friend Bourman (8) be read along with it for a more balanced view. The book with the best pictures is by Reiss (9); pictures are vital to understanding and appreciating a dancer whom one cannot actually observe.

The most authoritative biography of Nijinsky is by Buckle (10), and those who are seriously interested in the subject should begin there.

Ostwald's book is the best effort yet to describe and analyze Nijinsky's pathology. His clinical material was carefully accumulated and is valuable (if one considers the uncertain veracity of the sources), but his psychological analyses, especially in the early part of the book, tend to be quite speculative. For example, he writes, "Kirstein finds that the three ballets Nijinsky choreographed for Diaghilev parallel the sequence of psychosexual maturation proposed by Sigmund Freud: 'In *Faune*, adolescent self-discovery and gratification; in *Jeux*, homosexual discovery of another self or selves; in *Le Sacre de Printemps*, fertility and renewal of the race.'" Ostwald continues, "This is a valuable insight. It was in the course of working on these three ballets that Nijinsky actually tried to move away from his narcissistic position toward a more heterosexual orientation" (p. 62). Regarding *Le Spectre de la Rose*, Ostwald says, "Nijinsky invariably completed it by ascending in one of his most spectacular leaps that took him out the window (a symbolic and probably unconscious reenactment of his brother's catastrophic fall)" (p. 48). As with many psychobiographies, there is a kind of "jargonese" or popular psychology sprinkled throughout the text that some readers may find objectionable.

The strength and value of the book come especially for psychiatrists in its second half, where Ostwald focuses on the various diagnoses that were pinned on Nijinsky from time to time by a wide variety of hospitals, doctors, and "experts." From my point of view, this adds authentication to the impossibility of categorizing a breakdown in a genius of this magnitude within the usual psychiatric terminology. I do not think that the reader comes out with a clear idea of what happened to Nijinsky, not because Ostwald does not try but because there is no clear idea of what happened. Ostwald nicely documents the progression of authorities who attempted to apply their theoretical conceptions to this lovesick, exploited, misunderstood genius in their efforts to work with him, and I found myself depressed just reading Ostwald's interesting reports. There is something about extremely famous and creative individuals that draws authorities and experts to test out their theories; what is lost is the child within the patient who cries out not for investigation but for a therapeutic experience. Ostwald documents the pathetic mess quite well and introduces us to Nijinsky's wife, Romola, as a "camp follower" (p. 84) who "edits" or butchers Nijinsky's diary (5) in the tradition of Nietzsche's sister. Yet Parker (11, p. 177) calls her a heroine.

What happened to Nijinsky? An excellent description of the "trajectory" of his disorder is found on page 247. It is too long to quote in a review but lends itself to the valuable depiction of the psychotic artist by Arnheim (12). Such an artist recombines and restructures as he or she needs to, replacing a disappointing social world with the art medium. My picture of Nijinsky's Petrushka as a cross, with its mournful countenance of Don Quixote, says it all, and, as Arnheim suggested, the disintegration and alienation of modern artists like Nijinsky and Pound expressed our "botched civilization," as Pound called it. As the artist fragments, he or she employs genius in a haunting way *DSM-III-R* cannot capture, until finally it burns itself out and *DSM-III-R* is all that shows on the surface except for a sudden spectacular leap, or the Pisan Cantos, and the rest is silence.

In summary, I liked this book and found it entertaining as well as informative. I can recommend it as a study of Nijinsky's pathology by a conscientious psychiatrist, and the

author deserves our thanks and congratulations. It is also valuable as a humbling experience for all psychiatrists confronted with true genius, and it contains some sensible suggestions for the psychiatric treatment of artists who are not in the genius category. But the great book about Nijinsky remains to be written.

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Anne Sexton: A Biography, by Diane Wood Middlebrook. Boston, Peter Davison/Houghton Mifflin Co., 1991, 488 pp., \$24.95.

How can a mad housewife become a star? In her biography of the poet Anne Sexton, Diane Middlebrook mentions some things that help: Have a good psychiatrist. Have a mother-in-law who will take care of the kids. Yearn for fame. Work hard. Be lucky. Have talent.

The psychiatrist, in this instance, was Martin Orne. He was 29, a resident at Massachusetts Mental Health Center in Boston, when he first took on Anne Sexton as a patient. She was a year younger, a suburban housewife with two children and a husband who traveled. Her original diagnosis was postpartum depression. Over the next 18 years she had many diagnoses. She had suicidal depressions and mania, heard voices (at least once), went into trances, had amnesia and phobias, was hypersexual, neglected her children and sexually abused one of them, and had battered-wife syndrome—often all at the same time. She overdosed repeatedly and was in and out of nearly every psychiatric hospital in the Boston area during the 8 years that Orne saw her and the 10 years that followed. Her axis I diagnosis was probably bipolar disorder. Axis II? Anybody's guess. There probably should be a separate category for poets.

How did she become a star—probably, for a time, the most widely read poet in America? (Her books have sold more than fifty million copies. "I don't read poetry, but I read Anne Sexton," one fan said.) She won the Pulitzer Prize and other awards. A finishing school dropout, she became a university professor.

How did it happen?

Orne had been seeing her for a year and there wasn't much progress. Because of her trances (Orne considered her a clas-

sical hysteric), she couldn't remember one session from the next. He suggested taping their sessions so she could jog her memory. Then, one day, Orne asked if there was anything she felt she could do well. The only answer she came up with was prostitution. He suggested writing instead; maybe writing about her problems would help other people with theirs.

Write she did. In trances and manic furies, she turned out poems by the score, all neatly typed and shown to Orne and almost anyone else who would read them. She learned to write sonnets from a television educational program. She went to classes, joined poet groups, became friends and lovers with other poets. She impressed many as glamorous. She had been a model briefly as a teenager, and her leggy good looks survived alcohol and the ravages of time. As a wife and mother she was a mess, but as a poet she was a professional. She pushed her poems as ardently as a Hollywood agent. She became popular on the poetry reading circuit, asking for top dollar. In time she was making enough money from her books and poetry readings to buy a house and pool and afford an African safari.

She wrote about incest, masturbation, menstruation, and topics no one else would touch. She held back nothing about herself or her family. She was the ultimate of the confessional poets, out-confessing John Berryman and Robert Lowell. Many disliked her for this; others admired her. But most agree that at her best, forgetting the content, she was a good poet, in the top rank.

She was highly dependent on Orne, her surrogate for mother, father, and a great-aunt who loved to cuddle. (Cuddling was always a big deal with Sexton.) When Orne moved to Philadelphia, Sexton started a free-fall that ended in her death in 1974 at age 45. Her fame had increased steadily, but the quality of her poems declined, attributed by her biographer to alcohol, pills, too many lovers, Thorazine, and bad psychiatry. After Orne left she found another psychiatrist and did well for a time, but, as Orne delicately put it, she suffered when their "relationship" changed. With her divorce from her husband she lost another source of moral support. Then, one beautiful October day, she had a merry lunch with a poet friend, went home, stripped the rings off her fingers, put on her mother's old fur coat, drank some vodka, went into the garage, and started the car with the door closed.

This is a wonderful biography, holding back nothing, fair, and balanced. How does one produce a good biography of a poet? It helps if the biographer is a poet, as is Ms. Middlebrook. Hard work helps, and Ms. Middlebrook worked hard, interviewing 90 of Sexton's colleagues, friends, and family members. Finally, it helps to have access to 8 years of your subject's therapeutic tapes and notes, which Orne provided.

There's been a bit of brouhaha about the latter. Should Orne have done it? He had the family's consent. Self-revelation was Sexton's forte—no one doubts she would have approved. Orne didn't receive a penny in compensation.

For a true confessor, perhaps the more to confess about the better. If so, nothing could have pleased Anne Sexton more than this most revealing of biographies.

DONALD W. GOODWIN, M.D.
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A Question of Character: A Life of John F. Kennedy, by Thomas C. Reeves. New York, Free Press, 1991, \$24.95.

Thomas Reeves's *A Question of Character* became for me a question of scholarship. John F. Kennedy is certainly the

most heavily chronicled president of modern times, the written record of his life, brief reign, death, and family far outweighing that of many more accomplished chief executives. Although our fascination with this man seems bottomless, thoughtful people might wonder how much another biography can genuinely contribute. Because so much of what has been written, particularly in a negative vein, has appeared in such minimally reliable publications as Sunday supplements and supermarket tabloids, there remains a real need for a carefully documented biography meeting standards of academic historiography that will authoritatively balance conflicting allegations about J.F.K.'s personal life and character and their role in his presidency. Despite its claims of "extraordinary thoroughness" by "an experienced and respected historian and biographer . . . reading deeply in the primary as well as secondary sources," this is not the work for which we hoped, and as such adds nothing of value to the historical record. We have clearly gone well past the early hagiographies of Schlesinger and Sorensen, and perhaps even beyond the period of historic revisionism, which reassessed the Kennedy presidency from a greater distance and found elements of it insubstantial, secretive, vindictive, and marked by major blunders, most prominently characterized by the Bay of Pigs. Historians such as Professor Reeves are now testing on Kennedy the viability of the next approach for which Americans seem to have a considerable appetite, the frank vilification of its major political figures. The job has been completed on Nixon and Johnson and is well underway on Reagan.

Some of the anecdotes provided by Reeves concerning J.F.K.'s behavior, character, and motivations are indeed revealing, appalling, and even frightening, but virtually all have been printed before. There is a startling dearth of primary source material or other evidence of original scholarship here, and as a result the book commands no more authority than the work of the amateur historians on whom Reeves relies so heavily. Presented as a graduate student thesis in any major university history department, the book would earn an F. Reeves's hypothesis that character shapes actions and that the personal integrity of world leaders is a matter of concern for the general citizenry is inarguable and unoriginal. Perhaps much of what Reeves, a professor of history at the University of Wisconsin, Parkside, says concerning John Kennedy's obsessive adulterous womanizing and lack of consistent moral commitment is true, but the historical method necessary to establish such a record is as rigorous as the scientific method that our own profession relies on to confirm truth, and it is substantially absent from *A Question of Character*.

Professor Reeves quotes David Knowles's *The Historian and Character and Other Essays*: "The historian is not trying the men and women of the past." Nonetheless, Reeves proceeds as might a prosecuting attorney, putting the most unfavorable available interpretation on any and all of J.F.K.'s actions, sliding assumptions through as facts, and minimizing features of his subject's life and career that might argue against the book's general premise that Kennedy was a man of unremitting poor character protected from discovery by a still active propaganda machine which fooled all of the people all of the time. In his preface, Reeves writes that "several years ago" he "decided to examine the Kennedy history for myself, reading deeply in the primary as well as secondary sources . . . The result was this book." Reeves's deep reading in the primary sources produced, in the first six chapters (my patience for counting had limits, and the pattern became clear), 376 notes containing 729 citations. Of these 729 pieces of historical evidence, only eight are identifiable as genuine primary sources. There are 58 references to oral histories, which are

not actual primary sources as defined by historians because they rely on personal recollection of events years earlier, generally without documentary support. The remaining 671 (92%) of the citations are derived from earlier writers, with no fewer than 121 references in the first six chapters to *The Search for JFK*, a 1976 attack on the pre-presidential Kennedy by husband and wife team Joan and Clay Blair. Reeves notes that most of the work of the Blairs was based on documents in the J.F.K. Library, which he later criticizes as an unreliable source because he feels that it sequestered material unflattering to the President. Nonetheless, the J.F.K. Library appears to have been the only library Professor Reeves himself consulted, since no other library or archive is noted in his acknowledgments or citations. Other sources on which Professor Reeves relies are Kitty Kelley's *Jackie O!* (which he cites repeatedly after a mild caveat that this book, "designed for maximum sales, must be approached cautiously"), "Walter Scott's Personality Parade" in the Sunday supplement magazine, and a Kitty Kelley article in *People* magazine on Kennedy's reportedly mob-connected mistress Judith Exner.

Reeves cites "J. Edgar Hoover's private files" secondhand from William Safire's 1977 columns in the *New York Times*. Reeves notes that Safire obtained the files through the Freedom of Information Act; one wonders why Reeves failed to do the same and examine the primary source personally as a true historian would, rather than depending on an indirect citation. Reeves cites approvingly in his text information gathered by C. David Heymann in *A Woman Named Jackie* that Jack and Jackie had become dependent on amphetamines by 1961 but says in his notes elsewhere that he deeply distrusts Heymann's book. This critical assessment of sources is notably sparse elsewhere in Reeves's book. His lazy reliance on the published work of others is further apparent in his reference to a *Time* magazine article on a federal wiretap purportedly revealing conversations between mobsters concerning Kennedy's affair with Exner. Why would a legitimate historian rely on an article in the lay press rather than seeking the actual transcript of the wiretap? Can such work be called legitimate history?

The characterologic defects on which Reeves focuses could well have compromised the presidency. Although adultery among private citizens typically damages only the participants and their families, it can be posited that such behavior among those with vast responsibility could lead to blackmail and violation of the public trust. If Kennedy provided organized crime with access to the vast leverage of the White House, this would be egregious in the extreme. If he solicited financial and other support from organized crime and failed to reciprocate, he may have created conditions for the assassination that became one of the most painful experiences in the history of our national consciousness. The importance of Professor Reeves's premise, that the Kennedy character is well within the legitimate concern of Americans, demands a fully documented, intellectually rigorous accounting of our 35th president's motivations and behaviors. *A Question of Character* unfortunately does not meet these standards.

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Ludwig Wittgenstein: The Duty of Genius, by Ray Monk.
New York, Free Press, 1990, 654 pp., \$29.95.

For the psychiatrist interested in behavior, the biography of Ludwig Wittgenstein is a fascinating book. For the psychiatrist interested in history, the book creates a vivid and intense portrait

of the people, the intellectual issues, and the events leading up to two world wars. For the psychiatrist interested in philosophy, this book is a clear exposition of a philosopher's work that changed the field of philosophy and that greatly influenced philosophical thinking in the United States.

Ray Monk presents a very detailed, well-documented biography of Ludwig Wittgenstein. The picture presented of Wittgenstein and his colleagues, the Wittgenstein family, and the period is comprehensive and exciting. The Wittgenstein family was a glittering, wealthy, cultured Viennese family run by a tyrannical father; the mother was uninterested in the children. Three of Ludwig Wittgenstein's brothers committed suicide, and at one time the eight children had 26 private tutors. From this family environment emerged Ludwig Wittgenstein, whose life and career was most bizarre, completely fascinating, and of fictional stature. Wittgenstein, a rather shy, quiet student, was interested in aeronautics. In 1908, he enrolled in school to become an engineer in order to design and fly an airplane. During this time, he read Bertrand Russell's *The Principles of Mathematics* and became obsessed with philosophy. He went to England to study with Russell and impressed all of the philosophical giants at Cambridge with his brilliance. To the surprise of many, at the outbreak of World War I he joined the Austrian army and eventually volunteered for the most dangerous duty possible as an artillery spotter. It was during his 5 years as a soldier that he wrote his landmark work, *Tractatus-Logico-Philosophicus*. However, at the end of the war, rather than return to philosophy, he decided to become an elementary school teacher and attended school so that he could do this. Due to his father's shrewd investments, he was at that time one of the wealthiest people in Europe, until he decided to give away all of his money. He taught school in rural settings for several years and eventually returned to Vienna, where he set himself up as an architect. Subsequently, he returned to Cambridge, submitted the *Tractatus* as his thesis, and received both a Ph.D. and a Chair at Cambridge. During World War II he served as a hospital orderly and then again returned to his philosophical work at Cambridge.

These shifts in career and direction were carried out by a character structure that was ascetic, pristine, obsessive, and perfectionist, all colored by an intense depressive cast. Bertrand Russell described him as, "perhaps, the most perfect example I have ever known of genius as traditionally conceived, passionate, profound, intense, and dominating" (p. 46). Wittgenstein's intensity was such that people would dread his coming to visit or having to deal with him, but they were also drawn by his brilliance. His depressive cast and intensity are emphasized and portrayed best by a statement in a letter he wrote to George Maynard Keynes on his return to Cambridge: "We haven't met since eleven years. I don't know if you have changed during that time, but I certainly have, tremendously. I am sorry to say I am no better than I was, but I am different; and therefore, if we shall meet, you may find that the man who has come to see you isn't really the one you meant to invite. There is no doubt, that even if we can make ourselves understood to one another, that a chat or two will not be sufficient for the purpose, and that the result of our meeting will be disappointment and disgust on your side and disgust and despair on mine" (p. 223). These feelings contrasted with extreme narcissism, as manifested by the comment he made to G.E. Moore and Bertrand Russell when they examined him for his Ph.D. thesis on the *Tractatus*, "Don't worry. I know you will never understand it." (To some extent, they both admitted that they never did.) This made him a very difficult friend.

Monk presents this engrossing life in great detail. There is

little psychological interpretation or speculation; however, themes of ambiguous sexuality and feelings about his Jewish origins are often clearly implied as motivating factors in his behavior. Consequently, what emerges is a man with a single-minded nature who sought clarity and purity in almost everything he did. The description of Wittgenstein going to select furniture for his apartment in Cambridge, giving up completely, and having to design it himself is a clear comment about his drive for what he perceived as "perfection" and "simplicity."

The impact of Wittgenstein's character structure and his quest for clarity in his philosophical thinking, with which he never seemed to be satisfied, is clearly portrayed in this book. His views of the use of language and its relation to reality and his idea of what logical linguistic structures make it possible to decide what we can say and what we cannot say are clearly presented. Whether you have a philosophical background or not, these portions of the book will prove to be very exciting and interesting reading.

For a picture of the period, which included such luminaries as Bertrand Russell, Sigmund Freud, George Klimt, G.E. Moore, Brahms, and Mendelssohn, all of whom, in some way or another, touched and were involved with Wittgenstein and his family, it is wonderfully described, often in the person's own words. The passionate, humane, and sensitive persona of Bertrand Russell is also well detailed by Monk, which is a brilliant counterpoint to the pristine, ascetic, and obtuse interpersonal character of Ludwig Wittgenstein.

Each aspect of this book—the development and career of Ludwig Wittgenstein, the history of the period, and the philosophical expositions—serve to illuminate each other, creating a splendid and informative intellectual experience.

GARY J. TUCKER, M.D.
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Henry James and Edith Wharton: Letters: 1900–1915, edited by Lyall H. Powers. New York, Charles Scribner's Sons (Macmillan), 1990, 412 pp., \$29.95.

The letters that make up this volume were written between 1900 and 1915, a moment in the final flowering of Victorian England which ended when the Great War transformed Europe forever. Henry James was the literary master of his era, and he wrote Edith Wharton in his elaborate style, which always combined grace, elegance, and penetrating wisdom. In 1900 James was 57, an Anglicized American at the height of his productive career. He had written his classic novel *Portrait of a Lady* and was about to create *Wings of the Dove*, *The Ambassadors*, and *The Golden Bowl*, which represent the culmination of his efforts to render psychological portraits of characters ruled by anxiety, obligation, and the possibilities of love. Wharton, only 38, was also an American writer who lived mainly abroad, and she had sought out the relationship with James for many years without success. In 1900 she sent him a story that finally caught his attention, and she further struck a responsive chord by addressing him as "Dear Master." In James's letters he adopts the tone and style that enact the very role he had detailed in an earlier story, "The Lesson of the Master." His first letter entices the reader into the volume with its elegant and precise analysis of Wharton's story and of the author herself, with passages like this: "(It) has an admirable sharpness & neatness & infinite wit & point . . . only the tale is a little hard, a little purely derisive. But that is because you're so young, &, with it, so clever. Youth is hard—

& your needle-point, later on, will muffle itself in a little blur of silk." The unique quality of written correspondence is underscored by the attempt to imagine such remarks as these in any other form of communicative interaction.

Professor Powers' brief introduction and occasional interstitial remarks afford the reader a historical context for the correspondence, which consists in this collection almost exclusively of the letters of Henry James. Most of Wharton's letters fell victim to James's practice of periodically destroying his papers; thus, only 13 of the 176 entries are those of Wharton. What the editor provides us of the known details of Wharton's relationship with James is drawn from other sources, notably her published letters and her memoir *A Backward Glance* (1934). Considering the warmth of their correspondence it is surprising to learn that Wharton was often quite critical of James's writing. She once asked him, "What was your idea in suspending the four principal characters in *The Golden Bowl* in a void?" to which James quipped, "My dear—I didn't know I had." Their relationship rested on other foundations like shared social and literary experiences, and the letters document an ever richer friendship. Writing to Wharton obviously became for Henry James a sustaining commitment and pleasure, which was further deepened when Wharton's marital difficulties surfaced in 1908, leading her to commence an affair with one of James's oldest friends. She kept the affair secret from James initially but finally included him in her confidence. He remained her staunch supporter, offering advice and encouragement, now as another kind of "dear master"—devoted, benevolent, and avuncular. James's letter of 10/13/08 is his response to first learning of her affair and the disintegration of her marriage, and it contains a section that is a classic of wise counsel to the crisis-torn: "I am deeply distressed by the situation you describe & as to which my power to suggest or enlighten now quite miserably fails me. I move in darkness; I rack my brain; I gnash my teeth; I don't pretend to understand or to imagine. And yet, incredibly to you doubtless—I am still moved to say 'Don't conclude!' Some light will still absolutely come to you—I believe—though I can't pretend to say what it conceivably may be. Only sit tight yourself and go through the movements of life. That keeps up our connection with life—I mean of the immediate & apparent life; behind which, all the while, the deeper & darker and the unapparent, in which things really happen to us, learns, under that hygiene, to stay in its place. Live it all through, every inch of it, and out of it something valuable will come. But live it ever so quietly—and waitingly!"

For her part, Wharton comments on the nature of the relationship in her memoirs: "Perhaps it was our common sense of fun that first brought about our understanding. The real marriage of true minds is for any two people to possess a sense of humour or irony pitched in exactly the same key, so that their joint glances at any subject cross like interarching searchlights. I have had good friends between whom and myself that bond was lacking; and in that sense Henry James was perhaps the most intimate friend I ever had, though in so many ways we were so different."

The valence of need and resource in their relationship shifted with James's depression, poor health, and failing financial situation (literary success was no more dependable then than now). We learn of James's illnesses in 1910—digestive disorders and, most clearly, depression. He wrote of his need to travel and to get away from his home in Sussex: "to break as completely as possible with the sinister sense that my squeezed-in and boiled-down life (in this house) insidiously (entrapped) me these last 2 years." He consulted William Osler for his digestive disorder and, later, in the United States,

James Jackson Putnam for his depression. Neither was able to help him much. Wharton was deeply concerned, and in 1911 she attempted through friends to influence the selection of the Nobel prize for fiction in James's favor. She failed in that, but succeeded in 1912 in channeling some of her own money to him through the Scribner publishing house, disguised as a generous advance on an uncompleted work.

Despite progressive deterioration in his physical and mental state, James's letters to Wharton retained a buoyancy, especially in response to her letters from the front lines of the war in eastern France, which she visited in 1915. Half a year before he died, James complained to her of "an interminable gastric crisis of the most vicious and poisonous order. All the same . . . it has been a joy to know (of your adventures) and your magnificent time of life and force of activity (that) keep putting in your hand every anodyne of energy . . . I shall bless your news, and am your all-battered but all-affectionate old—Henry James."

These letters afford an almost microscopic glimpse of two gifted writers and their reflections on matters ranging from some too personal for the casual reader to comprehend to others that inform us incisively about manners, morals, concerns, and sensibilities of that day. It is a pointillist portrait that is as sociological as it is psychological. But more than anything else it is the diary of a warm and playful relationship bathed in crackling intelligence and wit. The uniqueness of this collection has much to do with its form, and while letter-writing isn't dead it appears moribund in the broad spectrum of communicative modes now visited upon us by the marvels of electronic technology. And so, in addition to its other virtues, works like this raise important questions about the definition of progress.

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Dickens, by Peter Ackroyd. New York, HarperCollins, 1990, 1,195 pp., \$35.00.

There are many reasons why psychiatrists should warm to this book. Those who apply diagnostic algorithms will find that Dickens met criteria for generalized anxiety disorder, conversion hysteria, posttraumatic stress disorder, obsessive-compulsive neurosis, major depressive episodes, and both an obsessional and a borderline personality structure. Those with an interest in psychodynamics and developmental continuities will appreciate the rich interleaving of his life story and his fictional world. All of us should appreciate Dickens as an agent of social change, recognizing how he mobilized the sensibility of the Victorian middle-class to the injustices faced by those trapped by poverty and other circumstances. We should also ask how successful we have been as a profession compared with Dickens in bringing sympathetic attention to the plight of the mentally ill and in providing them with a vision of a life that is possible. Peter Ackroyd records how Dickens succeeded—not as an intellectual radical but as a "radical by reason of his own position in society, and his own determination to transcend it."

Dickens inherited his mimicry, curiosity, verbal skills, and capacity for pathos from his mother. His father was regarded as affable, lazy, feckless, and with a veneer of grandiloquence hiding an unpredictable and fiery temper—an image that was to haunt Dickens. While his sister was sent away for a proper education, Dickens was sent to a blacking factory at the age of 12 to help the family's failing finances, a secret kept even

from his children. There he was surrounded by the "soil amorphous world of privation, of beggary and want," establishing the schema of the child "always in peril of being permanently consigned to the 'low' world from which he wishes to escape." Additional reason for scripting the fantasized secure family broken apart came when his father was arrested for debt and incarcerated in the Marshalsea Prison, evoking second schema of the innocent child left to fend for himself while carrying an overlay of guilt, shame, and humiliation.

A lonely child, with an extraordinary memory, visual imagination, and precognition even then—"morbidly sensitive horror, unable to stop listening, unable to stop reading, unable to forget"—Dickens processed such primal scenes into the motifs that were to be his signature. Such experiences also created his "outsider" status and, through this, his ability to observe and capture mid-Victorian society. He loved pantomimes and clowns—worlds where "no harm came to anyone . . . and conflicts . . . resolved in laughter." His writing captured his restitutive fantasies, with stories of innocent and gentle children forgotten and saved, of families reunited, of isolation conquered, of loss and return, as well as preoccupations with Christmas as symbolizing the "spirit of benevolence and family harmony." His public speeches and readings were attempts to unite the nation into his extended happy family by creating a community of love and to "reinforce his own sense of himself." Even when tired or frail he would come alive and bloom during a public reading ("like an organism through which an electric current is passed"), with audiences rapturous before he started and mesmerized by his performance. Dickens resonated with audiences. His seasonal Christmas books were symbols by which he and his "audience" could reaffirm the ties, and each gave the other life. Eventually, that strategy for "feeling alive" advanced his death. Self-object theory powerfully illustrated.

Ackroyd argues that Dickens was also driven by power—power over others, power to move and to sway, both in his voice and in his writings. Not surprisingly, he also revealed his anger against power bases, and Ackroyd notes Dickens' tendency "even when he is upholding the principles of social cohesion, to be at one with the rioters." Given power, he wielded generosity with instinctive charity to society's unfortunate and could be immensely caring. However, being driven more by instinct than by reason, he evidenced lacunae. He was a racist, would ridicule and caricature friends in his book and has been accused of "killing off" any interesting child merely to maintain the narrative. Blind and self-righteous in any such faults, with a need always to come out on top, he was quick to hurt and to strike out (his resolve in one instance being to "reform or ruin"), and, fearing failure, he was often watchful and afraid.

In his symbolic narrative fiction the images of his fragmented self-objects were reworked, together with alternatively abandoning or rescuing parent figures as well as benevolent or monstrous parent figures. Despite a publicly stated "belief" in the family, his fictional families demonstrated disunity, reflecting his early experiences of unreconciled emotional needs.

It was in the blacking factory that Dickens started to exert some control over his life, developing obsessional habits (such as making his money last all week by wrapping six parcels in coins, "each parcel containing the same amount and labelled with a different day"). In adulthood, obsessiveness was reflected in preoccupations with punctuality and with haphazard combining, in not being able to sleep unless the bed was in north-south direction, in touching certain objects three times "for luck," and in insisting on absolute neatness in his children.

with daily inspections of their rooms and regular written reproofs. Unless things were settled at once or "definitely arranged," he could not sleep, work, or eat. As a stage manager his style was "patience, perseverance, punctuality, order and neatness." As an observer, he was always scrutinizing, always examining. As a writer, the plot had to be perfected in his head before he "took up pen," and in his writing, everything went by clockwork, totally methodical and orderly. In his fiction, he built "order into the most disordered events" and worked through to a harmonious and tidy ending. Evident needs to control, dominate, and manipulate were also manifested in an ongoing fascination (and success) with mesmerism, as detailed in a biography reviewed in the *Journal* 2 years ago (1).

In the blacking factory Dickens also established a determination to rise above circumstances, to escape from poverty and social disgrace, and thus his philosophy of always striving, persevering, and enduring hard work, arguing that the "meaning of life came through labor." At 15 he became a junior clerk, learning shorthand and planning his next career as a political reporter, where immediately his concern with social injustices emerged. At 21 he started serious writing, and 3 years later commenced *The Pickwick Papers*, initiating the concept of serializing new fiction in a monthly journal and bringing to life "the most familiar, the most disagreeable and the most comic, elements of early nineteenth-century England . . . organised and controlled." He had immediate fame and a national audience because, as Ackroyd notes, his written "world" corresponded with the "deepest dreams and desires of his audience," giving his contemporaries a new sense of themselves. While writing *The Pickwick Papers*, he commenced *Oliver Twist*, the first novel in the English language with a child as its central character. These first two books demonstrated his gift for dialogue, for humor, and for characterization (especially the picaresque). Importing "melodrama and grotesquerie" from the stage, he respected the then-prevailing principle guiding the artist—to reflect the issues and mores of the time and to respect the social purpose of art—and, again, had almost immediate success. His use of "exaggeration and grotesquerie" in *Nicholas Nickolby* forced the closure of the infamous Yorkshire schools, allowing Dickens the satisfaction of affecting those very social conditions which had driven him.

Dickens was immensely driven, needing to "keep on with business and busyness" in his writings and readings, editing a weekly periodical for more than 20 years, constantly making trips, and having a "moral obligation" to walk as many hours as he worked. He once observed, "My only comfort is, in Motion."

Dickens' preoccupation with control had lacunae also. He loved speed as well as movement, and could be impulsive (he once leaned over the brink of Vesuvius, singeing his hair and burning his clothes). Just as control was balanced with impulsiveness, puritanical abstemiousness and rectitude dueled with his romanticism and sentiment. Predictably, real intimacy was difficult for him; he ultimately believed and trusted only in himself and kept his passionate nature too firmly under control, particularly in his writings (where "sexuality remains unconscious but everywhere apparent"). He was primed for a mid-life crisis.

He had escaped from social deprivation by worldly success and from his parents by rejecting them in his writings (what Ackroyd terms an "imaginative orphanhood"), but in mid-life Dickens became aware of a bitter deprivation. Public adulation had met only the more superficial needs for love. He observed to his early biographer, Forster: "How strange is to be never at rest, and never satisfied, and ever trying after some-

thing that is never reached." Feeling "neglected and hopeless" and with a sense of life closing down, he, who had idealized love, sought for it as "the one thing missing in his life." There had been an earlier attempt—besotted with his wife's younger sister, he had preserved her dress after her early death and wished to be buried with her. Now again his attempts were awkward, bizarre, and socially incompetent. He engaged in a "might have been" correspondence with an old girlfriend, Maria Beadwell, redolent with sentiment, remembering her as she had been 20 years before. But seeing her "toothless, fat, old and ugly" immediately shattered his fantasy, and his next essay mourned the loss of his first innocent love. At 45 he separated ruthlessly from his wife, portraying himself as the victim and misrepresenting the facts in a self-serving way.

Although details of Dickens' relationship with the actress Ellen Ternan have eluded all biographers, Ackroyd holds it unlikely that the affair was consummated. Instead, he says that the relationship was one of Dickens' most "enduring fictional fantasies"—sexless marriage with a young, idealized virgin.

Dickens was fascinated by circles, and Ackroyd traces several. He who had had a feckless and improvident father lived to see such characteristics repeated in the many tragedies and disappointments of his children. In a wry observation, Dickens noted that he "had brought up the largest family every known with the smallest disposition to do anything for themselves." Near death, he closed another circle. His final passage of narrative opens with, "A brilliant morning shines on the old city," while the first sentence of his first novel commenced, "The first ray of light which illuminates the gloom." As he wrote in *A Tale of Two Cities*, "as I draw closer and closer to the end, I travel in the circle, nearer and nearer to the beginning." Ackroyd's dissection allows the reader to appreciate Dickens' keen capacity to define and capture the continuity underlying much of human development.

Ackroyd has produced a rich biography, immensely perceptive and informed. The caveats are few. The book is far too long, and at times too detailed, often risking trivial pursuit. Ackroyd has a tendency toward purple prose. For example, in his description of Dickens retracing his neighborhood, he writes, "How terrible those memories must have been to him, then, to weep over the stones where his childish feet had trod." Ackroyd also tends sometimes toward rhetorical excesses: "never was a writer so exact, so thorough, so careful in his plans." In attempting to reject the view that biographers lack imagination, Ackroyd invokes a set of contrivances (e.g., imaginary conversations with Dickens), which, being in the Norman Mailer mode, have the advantage of making us aware of the effects on the "interpreter" but risk self-aggrandizement.

We lose no respect for Dickens as a great comic and poetic novelist, as a wonderful chronicler and social commentator, and as a fantasist of the highest order. Carlyle once criticized Dickens for providing "magic lanterns to amuse grown children." But, as psychiatrists, we know that adults still have a need for lanterns, magic or otherwise. Ackroyd allows us to understand the determinants of Dickens' tortured vision and its real-world manifestations—luminous energy and a need for the limelight, but a personality style that left others in the shadow.

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The Alchemy of Survival: One Woman's Journey, by John E. Mack, M.D., with Rita S. Rogers, M.D. Reading, Mass., Merloyd Lawrence (Addison-Wesley), 1988, 229 pp., \$18.95.

In his introduction, Dr. Mack writes of his first meeting with Dr. Rogers, the subject of this biography. In 1973, author and subject were introduced at a conference on the psychological aspects of the conflict in the Middle East. Over the course of their professional association, Dr. Mack learned of Dr. Rogers' life story, which, to him, dramatized the most important themes of their work in psychiatry and foreign affairs. He relates being moved by her personal story of survival: her Jewish background, her childhood in Eastern Europe, her courage while interned in a Nazi transport camp in the Ukraine, her escape from two Communist regimes, and her eventual emigration to a new life in the United States. Despite personal hardships, she graduated from medical school in Vienna and, soon after arriving in the United States, completed her psychiatric residency training. She is currently a clinical professor of psychiatry at the University of California, Los Angeles, a practicing child psychiatrist, and a leader in the field of psychiatry and foreign affairs. The book was written by Dr. Mack with the "active participation" of Dr. Rogers. His stated purpose was to relate not only a story of survival but also an example of the transformation of traumatic experiences into an aspect of a productive and healthy life. In this purpose Dr. Mack succeeds. However, the reader is left with a sense of being denied an in-depth look at the complexity of Dr. Rogers' life and therefore of having an incomplete understanding of her character.

The story begins in Radauti, Romania, the birthplace and childhood home of Rita Rogers, born Rita Stenzler. Her early years were characterized by financial stability for the Stenzler family: Rita and her sister Nora are described as pampered and spoiled. Much of the book is devoted to this early period: to Dr. Rogers' family life and the Jewish community that fostered her sense of belonging and identity. It is this childhood stability (both financial and psychological), Dr. Mack maintains, that led to the inner strength necessary to survive subsequent tragedy. As the political climate changed in Eastern Europe in the 1930s, so did the life of the Stenzler family. Dr. Mack adds relevant and interesting background historical data while never losing sight of the impact these events had on the lives of Dr. Rogers and her family.

The book goes on to describe the years at Mogilev Podolskiy, a Nazi transport camp where the Stenzler family was interned between 1941 and 1944. Although the family remained together, the threat of separation and death was present in their daily life. Despite the hardship, Dr. Rogers exhibited courage, intellectual curiosity, and even a bit of recklessness and bravado that allowed her to preserve some optimism. Her initiative in becoming a foundry worker (she convinced a master foreman to slip her into the foundry at night in order to teach her the necessary skills) probably saved her family from deportation and death. This was also a period when she was exposed for the first time to people of different languages and cultures. The insight gained in these experiences appears to serve her well in her present work.

Dr. Rogers spent the turbulent postwar years in a variety of different roles and locations: from secretary at a music school in Czernowitz to medical student in Prague and Vienna and finally an émigré in the United States. The events since her immigration, including her marriage and her professional development, are briefly summarized in the remainder of the book. Her interest and work in foreign affairs are outlined in

more detail than are the more personal aspects of her adult life.

This is an inspiring story, but one told from a respectful distance. In his introduction, Dr. Mack writes of Dr. Rogers' belief that "some suffering . . . must remain private" and of the unusual and delicate situation of an author whose subject is a colleague and friend. Making these difficulties explicit unfortunately does not negate the problems they engender. The book reads like a benign chronological retelling of events without the intimate emotional touches necessary to fully appreciate Dr. Rogers' character. Her personal life since reaching the United States seems off limits. Unanswered questions about her earlier life leave the reader somewhat confused. For example, we wonder about the nature of the relationship between Dr. Rogers and her sister Nora. Why was there an abrupt termination of the friendship of Dr. Rogers and Ellen Davidson, her best friend from Mogilev Podolskiy? Why did Dr. Rogers choose to emigrate to the United States instead of to Israel, where her family had settled? With this book, Dr. Mack captures the imagination but not the heart.

Finally, an intriguing aspect of this collaboration is a journey referred to by the author throughout the book. (Is this the journey of the title?) Much of the data were collected from conversations between the author and subject during travel (which also included Dr. Rogers' daughter Sheila and Dr. Mack's son Kenneth) to Dr. Rogers' birthplace, to the camp where she was interned, to Prague and Vienna, where she was a medical student, and to places in the United States. Dr. Mack hints at the emotional impact of these visits on Dr. Rogers but unfortunately does not elaborate. For example, the reverence with which her early years are portrayed and the subsequent disappointment Dr. Rogers experienced in returning to her birthplace suggest a common human experience often portrayed in literature and exemplified in George Seferis' poem "The Return of the Exile" (1): My old friend, what are you looking for? After/years abroad you've come back/with images you've nourished/under foreign skies/far from your own country.

If Drs. Mack and Rogers wished to chronicle this journey (perhaps including its effects on them and their children), they would find an enthusiastic audience in myself.

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The Key to Genius, by D. Jablow Hershman and Julian Lieb M.D. Buffalo, N.Y., Prometheus Books, 1988, 220 pp. \$21.95.

When asked to review a book so grandiosely titled, I was intrigued and just a little suspicious. The title promises so much. So I was surprised and delighted as I began to page through Hershman and Lieb's superbly written narrative and follow the authors' attempt to unravel the Gordian knot linking madness to genius.

The book's opening sentence reads, "We define genius as the proven ability to produce artistic, scientific, or other intellectual work that is considered supremely valuable during or after the lifetime of the producer" (p. 7). The authors are interested in the fundamental driving forces of genius, and, in

particular, they explore how manic-depressive illness touches and often augments the creative experience in talented individuals. They believe that manic energy cycling with depressive introspection intensifies the creative process and that mania—when harnessed—may simply be what is commonly called “the creative urge.” Manic exuberance provides the confidence and defiance of criticism that are indispensable when charting new frontiers, and depression offers the self-examination and pursuit of perfection required to refine inventive works.

Sprinkled throughout this book are countless historical illustrations framing the authors’ discussions of genius, manic-depression, and creativity. Chapters three, four, five, and six make up the bulk of the book and offer fresh medical views on the lives of Newton, Beethoven, Dickens, and Van Gogh, each a creative genius, each manic-depressive. These original psychobiographies clearly portray the clinical and creative manifestations of mania and depression. The authors innovatively explore the largely untold story of how manic-depression augments creativity and the costly price a talented person pays for this “creative edge.” As a lagniappe, each biographical chapter is adorned with a skillful and not too broodingly psychological pen-and-ink portrait drawn by Hershman.

Throughout *The Key to Genius*, eminent historical personalities keep popping up, many names I remembered from undergraduate studies and more recently chanced upon when browsing back aisles of bookstores. So I was curious why the authors chose Newton, Beethoven, Dickens, and Van Gogh to exemplify manic-depression and creativity. Van Gogh, surely, but why the others? It became clearer as I read.

For Sir Isaac Newton, mood abnormalities began in childhood; later, his university years at Cambridge were characterized by depression, an abstemious disposition, and hard work. Like Beethoven, Dickens, and Van Gogh, his moods cycled with the seasons, and mania often launched him into new scientific ventures, inflaming him with the confidence to undertake problems of universal dimension: gravitation, the nature of light, and the invention of differential and integral calculus. Mania defies constraint, and Newton’s manic *Wel-tanschauung* ranged from mathematics to miracles (he filled 17 books with religious writings). Like other individuals with manic-depression, Newton had a contradictory temperament throughout his life as the polarity of his illness offered him opposing perceptions of reality.

Geniuses are never easy to live with, but living with Ludwig van Beethoven was unquestionably impossible. He was manic-depressive, deaf, paranoid, arrogant, scruffy, and alcoholic. Eventually he drank himself to death. Hershman and Lieb accurately recognize that the women who loved him had much to overlook. Like most great artists, he sought love and certainly sensed love was essential to his creativity, but like Newton, Van Gogh, and other geniuses, he found affirmation only through his creative process, leaving his music as the best portrait of his moods.

Keeping pace with Charles Dickens was hard, even for his spouse, who was also manic-depressive. Dickens was insomniac and relentlessly hyperactive. He openly admitted an attraction to “mad people,” and in life and fiction, Dickens was most comfortable among the offbeat. In childhood he suffered the torments of destitution, but by his early 20s, he was already a nineteenth-century superstar. Literary notoriety, wealth, boundless energy, and wild sways of emotion launched him into a speciously endless “fast lane.” Mania seemed his natural disposition, but when caught in depression’s darker moments he visited morgues. There is little known about his drinking habits, but toward the end of Dickens’ life, he, like Beethoven and Van Gogh, was alcoholic.

Dickens knew fame early, but Vincent van Gogh was another story. His life was a haunting tragedy and his every endeavor scorned. It is tempting to suggest that Van Gogh was simply ahead of his time, but the fact is there would never be a comfortable time or place for him. His self-punishing asceticism, fear of success, identification with outcasts, and storm-tossed mind would always bar him from the mainstream. His brother Theo once wrote, “As you know, he has long since broken with what is called convention. His way of dressing and his manners show directly that he is an unusual personality, and people who see him say, ‘He is mad’ ” (p. 161). Another historical view of Van Gogh’s “madness,” separate from that of the authors, surrounds suspicions that he suffered from partial complex seizures, which might have caused his rages, perceptual distortions, and the hypergraphia observed through his compulsive letter writing to Theo.

Vincent van Gogh was remarkable in still another way—he was one of the few geniuses that seemed genuinely unaware of his immense talent. Genius, like beauty, is seldom invisible or worn unknowingly, but Vincent van Gogh was, in so many ways, naively innocent.

The Key to Genius may be faulted only for shyness in not searching other pathways to genius. The idea of innovative psychopharmacotherapy emphasizing modulation of mood to enhance creativity is too hastily examined. Hershman and Lieb certainly uncover part of the mystery surrounding the term “mad genius,” and manic-depression truly may be the springboard from great talent to absolute genius; one truth is rarely the whole truth. The book is not psychoanalytically overdetermined, but biographies must always be suspect in the light of the author’s slant (1). For instance, the story of Dickens suggests and the biographies of Beethoven and Van Gogh mandate dual diagnoses including alcoholism. This is hardly unusual. When searching for a “creative leap,” many geniuses and lesser talents have sought the quick release of alcohol and other intoxicants to break their link with convention. The strength of this book is its solid contribution to the thesis that affective disorders may be as much a hereditary gift as a hereditary taint (2).

This splendidly written book has a brisk flow and is clearly organized to be enjoyable and informative. The bibliography is 14 pages long, and even though it is formidably and eclectically researched, the book never suffers from overly intrusive scholarship or impeding structuring devices. Every page is tightly written, citing some historical instance or pertinent quote contributing to the authors’ thesis that manic-depression is the gateway to genius. The writing is closer to a historical narrative than a medical textbook. For those psychiatrists interested in creativity and biography and are already comfortable with the signs and symptoms of mania and depression, this little book would still be an informative and valuable addition to their medical and literary bookshelves. *The Key to Genius* is not a mere mustering of drab case studies but, rather, a novel look at the long-term impact of affective disorders on the lives of geniuses and other eccentric visionaries.

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PHILOSOPHY

Philosophy, Psychiatry, and Neuroscience: Three Approaches to the Mind. A Synthetic Analysis of the Varieties of Human Experience, by Edward M. Hundert. New York, Clarendon Press (Oxford University Press), 1989, 338 pp., \$49.95.

The three disciplines in the title say much about this book's subject matter but little about its method. From philosophy Hundert brings traditions of criticism, reflection, and synthesis; from psychiatry, science in search of human betterment; from neuroscience, striving for reliable biological knowledge. These three approaches to the mind reprise the title and broad reach of his mentor Leston Havens' work (1). Nevertheless, the methodological soul of this book is philosophy.

I must admit considerable admiration for Hundert's wide-as-the-sky scholarship. The joyful audacity of his concept is more suggestive of a rude Texan than a tweed and button-down New Englander. Somehow the enthusiasm of a natural teacher creeps into his *prim exegesis*. Like a scorpion in a morning slipper, you are stung before you know what's happened.

The task faced by Dr. Hundert would seem numbing. His response to a conceptual assault from Kantian and Hegelian philosophy, Freud, Piaget, Minkowski, Fodor, Edelman, et al., is to translate and organize an intellectual melting pot into a meditation on the epistemic interdependence of brain, mind, and world. He calls his task a synthetic analysis. From Descartes he draws the original problems: How can we gain knowledge or truth about the world? How can we have mental experience with our material body? From Kant and Hegel he shapes a conceptual and methodological core: the dialectic that knowledge is subject-dependent *and* object-dependent. From Piaget and Freud he gains a developmental perspective and establishes the necessity for other people in developing

knowledge. From Fodor and Edelman he gains some biological clues to the relationship of mind, brain, and world. Hundert concludes, "By embedding its dialectic [of mental states and environment], not merely in self-conscious individual experience, but in biologically grounded cognitive mechanisms which by definition apply equally to all members of the species sharing our everywhere-and-unavoidable world, the Synthetic Analysis establishes the possibility of intersubjective human knowledge as an internal solution to the foundational problem of epistemology" (pp. 296-297; original is italicized). In the process Hundert 1) reviews a lot of modern philosophy, contemporary cognitive neuroscience, and twentieth-century psychiatric theory and 2) provides a thorough and historical argument for a scientific and conceptual pluralism.

Whew. This book must have been ambitious for the author, and it is an ambitious read. To his credit, Hundert has added some thoughtful touches, such as an orienting introduction and final summary, end-of-chapter citations, and a comprehensive bibliography. Philosophers particularly may take issue with some of his interpretations and conclusions, and I have my share of reservations myself, even for some of the psychiatry here. All in all, however, Hundert's work is laudable. In the current environment of ever-so-specialized research and thought, interdisciplinary works such as this one will orient serious students and shape future knowledge.

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Reprints of Book Forum reviews are not available.

Caution With Use of Tricyclics in Patients With AIDS

SIR: The following case illustrates the importance of caution and the principle of "start low, go slow" in using tricyclic antidepressants for patients with suspected AIDS (1) and other medical illnesses, as has long been noted for elderly patients (2).

Mr. A, a tall, abnormally thin, anxious 42-year-old man, had his first psychiatric hospital admission with complaints of depression including dysphoria, difficulty concentrating, poor sleep, and weight loss. His mother also expressed concern that he wandered the streets at night. He initially denied risk factors for HIV infection, which we suspected because of 1) his history of vague, chronic poor health, 2) the combination of psychiatric, organic mental, and general physical problems (problems with concentration and attention, managing day-to-day activities, relative lethargy and apathy), 3) his normal initial laboratory test results with the important exception of a low WBC count of $2500/\text{mm}^3$, and 4) the increasing incidence of such illness seen in our community mental health center in an inner city catchment area.

Mr. A agreed to HIV testing. After a 5-day observation period without response to good general medical care, and with Bender and MMPI test results indicating depression, nortriptyline was started at 25 mg h.s. and was increased over 3 days to 75 mg h.s. Over a period of 2 weeks, the patient improved, first with better sleeping and eating (he asked for and consumed "double portions") and then with improvement in dysphoria, smiling, increased spontaneity, and participation in activities. However, one night he reported seeing snakes in his bed and agitatedly persisted in searching for them. Nortriptyline was stopped, a check of his nortriptyline level was ordered, and a low dose of haloperidol was started. The nortriptyline level was 513 ng/ml, and a few days later it was 170 ng/ml. An ECG was borderline abnormal, with perhaps some marginally increased P-R interval. Mr. A's psychotic symptoms disappeared.

In the meantime, information to support the diagnosis of HIV infection, such as a history of homosexuality, recent herpes zoster radiculitis, and oral thrush infection, was noted. The HIV test results (both ELISA and Western blot) were positive, and repeat test results were also positive. Mr. A greatly improved with combined psychiatric and AIDS treatment, including zidovudine (AZT).

This patient never received more than 75 mg/day of nortriptyline and initially seemed to tolerate this well, with improvement. If depressive symptoms had recurred, we would have tried psychostimulants, preferably methylphenidate (3, 4). At times, psychostimulants have been reported to be effective in the rapid remission of depressive signs and symptoms in other medically ill populations (5). Fernandez (3) has stated, "The general psychostimulant experience with HIV patients is highlighted by psychomotor activation, appetite stimulation, and qualitative improvement in higher cortical functions (such as attention, concentration, memory and information processing) and in affect within hours."

The overlap of the symptoms of depression and subcortical dementia in this patient should be noted. Also noteworthy is his initial denial of high-risk behavior associated with HIV infection. Mr. A had consulted nonpsychiatric physicians during the previous year for isolated conditions, and HIV infection had not been diagnosed. Also, "neuropsychiatric disorder is the initial clinical disease manifestation in 10%–25% of HIV-infected persons" (1). As always, we must remain alert.

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Methadone and Schizophrenia

SIR: In recent years the treatment of schizophrenia has focused on new agents marketed to treat this chronic disease. The role of exogenous and endogenous opioids in schizophrenia has received little attention. In 1985 the *Journal* published a pilot study of the efficacy of methadone and neuroleptics in combination as a treatment for schizophrenia (1). We report the case of a patient with schizophrenia who responded to an increasing dose of methadone.

Mr. A, a 34-year-old man, had suffered from auditory hallucinations, bizarre delusions, and paranoia since adolescence. Despite his symptoms, he managed to be accepted into the military, where some years later he became dependent on drugs and alcohol. He was primarily dependent on alcohol until he became sober 6 years ago, at which time he began abusing heroin intravenously. Mr. A reported that his initial euphoria from heroin ceased, and he began to use heroin as a "self-medication" to lessen his prominent auditory hallucinations. During his 6 years of opiate dependence, he went through numerous methadone detoxification and maintenance programs but relapsed as his symptoms of schizophrenia increased. He was referred to the Veterans Administration (VA) from a community methadone maintenance program when he reported to its staff that he was hearing voices. Apparently, that program did not treat psychosis.

At the time of referral, Mr. A was taking 40 mg of methadone and had been taking that dose for the past 2 weeks. A detailed initial assessment showed that he clearly met the *DSM-III-R* criteria for chronic paranoid schizophrenia and opiate dependence. The methadone was continued, and he was started on various neuroleptics. Dystonia and severe akathisia ensued, even with maximal antiparkinsonian medication. Since he could not tolerate even low and divided doses of low-potency neuroleptic medication, it was decided, with the patient's consent, to attempt to use methadone in increasing doses as the sole antipsychotic. Over the course of 5 weeks, Mr. A's dose of methadone was increased from 40 mg to 80 mg (increments of 10 mg per week). His Brief Psychiatric Rating Scale (BPRS) score decreased in a linear fashion from 70 originally to 30 about 5 weeks later, when he was taking 80 mg of methadone. On follow-up at 3 months, Mr. A was still taking 80 mg of methadone and had a BPRS score of 31.

The use of methadone in the treatment of schizophrenia has been advocated in selected cases (2). The most serious argument against the use of methadone in schizophrenia is ethical (3). Iatrogenic opiate dependence was not an issue in our patient, because methadone was already part of the treatment plan for his opiate dependence. Extrapyramidal side effects prevented the use of neuroleptics, and clozapine was not available at our VA hospital.

The literature suggests that the comorbid diagnoses for narcotic addicts are predominantly depression and personality disorders (4). Our case illustrates the dual diagnosis of schizophrenia and opiate dependence and how methadone can be used in selected cases as the sole treatment for both disorders. In addition, we believe that there is a proportion of opiate-dependent individuals who self-medicate for schizophrenia and that this rather old treatment for psychosis should not be forgotten.

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Safety and Efficacy of Fluoxetine

SIR: Recent case studies have linked fluoxetine with patients' suicidal preoccupations (1). Our hospital's psychopharmacology consultation committee reviewed our experience with fluoxetine following these reports.

We had treated a diagnostically heterogeneous group of 50 severely and persistently mentally ill patients with fluoxetine. No patient experienced the onset of suicidal thoughts or behavior following fluoxetine treatment. Fourteen of the 50 patients had had documented suicidal thoughts or behavior before taking fluoxetine, and in no case were such thoughts or behavior worse while receiving fluoxetine. Thirty-seven of these 50 patients substantially improved with fluoxetine.

We conclude that fluoxetine is a safe and effective medication for hospitalized patients with severe and persistent mental illness.

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DEBRA HARRIS, M.D.
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Postpartum Psychosis and Mastitis: A New Indication for Clozapine?

SIR: It was with great interest that we read the letter by Uehlinger and Baumann (1) on clozapine as an alternative treatment for neuroleptic-induced gynecomastia. In contrast to other neuroleptic drugs, clozapine does not cause permanent elevation of serum prolactin levels (2). We have exploited this special pharmacological profile of clozapine (3) in another clinical setting, the management of postpartum psychosis in a lactating patient with mastitis.

Ms. A, a 28-year-old woman, was referred to our department for further management of paranoid postpartum psychosis diagnosed 1 week after delivery of a healthy daughter. The patient's pregnancy had been uneventful, and her psychiatric history was unrevealing. Following administration of zuclopenthixol decanoate, 600 mg, she had developed severe extrapyramidal side effects. Concurrent mastitis was treated with bromocriptine, 7.5 mg. On admission, bromocriptine was withdrawn. Clozapine, at a final dose of 200 mg, was slowly substituted for zuclopenthixol decanoate because of clozapine's strong antipsychotic potency (3), its lack of extrapyramidal side effects (3), and its negligible influence on serum prolactin levels (2). With this regimen, both the mastitis and the paranoid psychosis remitted within days.

The pharmacological treatment of postpartum psychosis within the lactation period is a complicated issue for several reasons. First, inhibition of lactation by bromocriptine is a therapeutic goal but may not be feasible because of bromocriptine's psychotogenic potency. Second, the rationale for treating mastitis with a dopamine receptor agonist, bromocriptine, with concurrent use of potent dopamine receptor antagonists is questionable and has not been thoroughly investigated. Third, continuous application of neuroleptic drugs maintains high serum prolactin levels and may be contraindicated in florid mastitis. In conclusion, we suggest that clozapine should be considered the drug of choice in postpartum psychosis with lactation and/or mastitis.

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Anticholinergic Delirium Caused by Retreatment With Clozapine

SIR: The need to titrate the dose of clozapine slowly when initiating treatment, because of its atypical side effects, has been previously reported in the literature (1, 2). A case of clozapine-induced delirium caused by a large initial dose of clozapine has also been reported (3). We present a case showing the importance of slowly titrating clozapine when reintroducing the medication in a patient who has previously tolerated higher dosages of the drug, even after a relatively short hiatus in treatment.

Mr. A, a 22-year-old man with chronic schizophrenia, who was on a research protocol, had not responded to multiple neuroleptic trials before starting clozapine. He responded well to clozapine, with resolution of his psychotic symptoms at an oral dose of 200 mg b.i.d. Approximately 6 months after the remission of his symptoms, his medication was tapered and discontinued over a 3-day period as part of the research protocol. No adverse effects occurred during the withdrawal period.

After a 17-day drug-free interval, clozapine was restarted as specified by the research protocol, but at an inadvertently large oral dose of 200 mg b.i.d. Twenty-four hours later, Mr. A complained of nausea, generalized weakness, and urinary hesitancy. Thirty-six hours after restarting clozapine (after four doses), he developed profuse diaphoresis, lightheadedness upon standing, mild diffuse abdominal pain, and delirium. Clozapine was immediately discontinued, and the patient was referred to an emergency room for medical evaluation.

Examination in the emergency room revealed the following vital signs: oral temperature, 99 °F; blood pressure, 110/70 mm Hg; pulse, 100 bpm; respirations, 22/min with mydriatic pupils and diaphoresis. On abdominal examination, Mr. A exhibited diffuse, nonspecific abdominal tenderness, mild distension, and hypoactive bowel sounds. He remained delirious.

Laboratory results revealed a WBC count of 12,200/mm³ (normal range=4,000-10,000/mm³), with 82.3% granulocytes, and a serum amylase level of 154 U/liter (normal range=34-122 U/liter). Flat and upright abdominal X-rays disclosed a nonspecific gas pattern and a large amount of stool in the colon. The emergency room physician's diagnosis was an adverse reaction to clozapine. The patient was admitted to a psychiatric unit for further observation. Additional laboratory results indicated a total hyperbilirubinemia of 1.8 mg/dl with a direct bilirubin of 0.2 mg/dl.

Fifteen hours after Mr. A's last dose of clozapine, the fever, abdominal tenderness, generalized weakness, and diaphoresis gradually resolved. The delirium and tachycardia cleared within the next 9 hours. Over the next 3 days, his leukocytosis, hyperbilirubinemia, and hyperamylasemia resolved. There was no recurrence of his psychotic symptoms during the period of drug discontinuation and delirium. He was then discharged from the hospital, and over the next 2 months, clozapine was restarted and the dose was

gradually titrated to 150 mg b.i.d. The patient remained free of delirious or psychotic symptoms.

This patient experienced acute symptoms of an anticholinergic syndrome (delirium, decreased gastrointestinal motility, tachycardia, and urinary hesitancy), antiadrenergic symptoms (orthostatic hypotension), hyperthermia, transient drug-induced hyperbilirubinemia and hyperamylasemia, and mild generalized peritoneal irritation after reintroduction of clozapine at a moderate and previously well-tolerated dosage. These acute symptoms contrast with those of classical neuroleptics, that is, extrapyramidal effects and dystonic reactions (2).

This case report illustrates that another distinctive characteristic of clozapine, unlike classical neuroleptics, is that the achieved tolerance of the antiadrenergic and anticholinergic effects of the drug does not persist when the medication is discontinued, even if only for a brief period, and then restarted. We recommend a low starting dose and gradual titration when restarting the medication in patients who have undergone drug-free intervals during their clozapine treatment.

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Should Postattack Phenomena Be Included in the Definition and Description of a Panic Attack?

SIR: The phenomenology of panic attacks has been a relatively neglected area of study. There is one aspect of panic attacks that has received even less attention, although it may be important for adequate conceptualization of the disorder. I present here the results of a pilot study of postattack symptoms and experiences.

Fifty-four subjects with panic disorder were evaluated by means of a structured diagnostic interview (1) and an interview eliciting information about the symptoms that the subjects usually experience during and *immediately after* their panic attacks.

Only 12 (22%) of the panic patients reported that they usually felt well after the attacks. Thirty-nine (72%) described fatigue as their common postattack experience. Almost one-half (26 patients) usually felt relieved. Fifteen (28%) of the patients described continued anxiety, and seven (13%) reported that they were specifically apprehensive about the possibility of another panic attack. Depressed feelings were reported by 14 (26%) of the patients, and various somatic symptoms were described by 11 (20%). Eight patients (15%) reported feelings of confusion and interference with thinking, and eight patients, too, were usually preoccupied with feelings of embarrassment, shame, or humiliation. For seven patients, angry feelings were their common postattack experience. Finally, three patients (2%) mentioned that they usually felt lethargic or sleepy.

Although postattack experiences are not uniform, it is striking that the great majority of these panic patients reported feelings of fatigue immediately following a panic attack. The common occurrence of fatigue following panic attacks has been observed, albeit in an unsystematic manner, by other authors also (2, 3). The way in which fatigue was described by patients in this sample seemed characteristic; they reported feeling "exhausted," "drained," "wiped out," "wasted," "washed out," "run down," "worn out," "weak," or having no energy at all. All of these terms suggest a mental and/or physical *depletion* as the basis for their feeling of fatigue. Also common was a combination of fatigue and emotional relief.

The obvious question is whether postattack fatigue reveals something about the nature of panic attacks. For example, can fatigue with the seemingly characteristic, aforementioned features be conceptualized as a consequence of an overwhelming autonomic nervous system discharge? Is there any relation between postattack fatigue and the feeling of lethargy that usually follows seizures (2)?

Unfortunately, the feeling of fatigue is still a poorly understood phenomenon, partly because it has many different meanings. On phenomenological grounds, however, it seems warranted to include postattack fatigue in the description of a panic attack and perhaps to include it in the corresponding diagnostic criteria as well, along with the provision that fatigue does not have to be present in all patients with panic attacks. Further research is necessary to determine the prevalence of postattack fatigue in larger samples of panic patients and to shed more light on its origin.

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Seasonal Worsening of Bulimia Nervosa

SIR: "Seasonal affective disorder" refers to recurring episodes of major depression or mania with a change in season (1). Bulimia nervosa may precede, follow, or occur with the onset of major depression (2). We treated two patients with seasonal affective disorder who experienced the occurrence or worsening of bulimia with the onset of major depression in September.

Ms. A, a 38-year-old woman, had experienced the onset of major depression every September since she was 19 years old. She spontaneously recovered every March. Her symptoms included depressed mood, anhedonia, lack of reactivity, forgetfulness, poor concentration, hypersomnia, and hyperphagia.

Ms. A reported that she binged and purged less than once weekly in the spring and summer but that she had been binge eating and purging "at least" six to eight times daily when she presented in September. This change in the

frequency of these behaviors was a recurring annual pattern for Ms. A.

The severity of Ms. A's depressive syndrome decreased, and the frequency of binge eating and purging fell to once weekly in the course of treatment with tranylcypromine. However, she left treatment before experiencing the maximum efficacy of tranylcypromine (3).

Ms. B, a 24-year-old woman, had experienced the onset of major depression every September for 10 consecutive years. She spontaneously recovered in April. Her symptoms included depressed mood, loss of interest, anhedonia, hypersomnia, psychomotor retardation, impairment of concentration, and suicidal ideation. Ms. B also binged and purged about six times weekly when depressed.

Ms. B's Carroll Rating Scale for Depression (4) score was 26 (moderately severe) before she started treatment. She began to take 20 mg/day of tranylcypromine, and her depression score fell to 3 (within normal limits) by day 35 of treatment. She also ceased to binge eat and purge.

Tranylcypromine was discontinued in the spring, but Ms. B returned in September in the midst of an episode of major depression. Her Carroll Rating Scale for Depression score was 24. She reported that she had started to binge eat and self-induce emesis about four times weekly a few weeks earlier. She added that she was not pleased with her response to treatment the previous winter. Consequently, her daily dose of tranylcypromine was raised to 30 mg over a period of 3 days. Her depression score was 7 on the 16th day of treatment. Her daily dose of tranylcypromine was increased to 50 mg on the 20th day of treatment because of fatigue and hypersomnia. She ceased to binge and purge within 10 days. Her depression score was 2 on the 25th day of treatment.

On the basis of routine and clinical structured interviews (5), both patients met the criteria for major depression with a seasonal pattern and for bulimia nervosa. The relation between the onset and remission of fall/winter episodes of major depression and the symptoms of bulimia nervosa is interesting. Ms. A's binges and purges decreased from six to eight times daily to once weekly despite her leaving treatment prematurely. Ms. B had major depression with a seasonal pattern of bulimia nervosa. The symptoms of both disorders were highly responsive to tranylcypromine (3).

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Unsolicited Reports of Sexual Abuse in a Comparative Study of Treatments for Bulimia

SIR: The relation between childhood sexual abuse and later development of eating disorders has recently been a focus of research. While it was not an aspect of our comparative study of treatments for bulimia, a serendipitous finding emerged regarding this relationship. Thirty-nine bulimic women were randomly assigned to a behavioral, a cognitive behavioral, or a nonspecific control condition. Subjects were seen individually, weekly, during the 8-week program by a male or female master's-level psychologist. Therapists were counterbalanced across conditions. Pre-treatment one-way analyses of variance revealed no significant between-group differences on demographic, behavioral, or psychological measures and no significant group differences in perceptions of the therapists.

Assessment measures and interventions did not address childhood sexual abuse and were not intended to elicit information concerning sexual abuse. Nonetheless, 49% (19 of 39) of the female bulimic subjects spontaneously reported having been sexually abused. There were no clear differences between subjects' rates of reporting sexual abuse to the male and the female therapist. Hall et al. (1) and Root et al. (2) indicated that 50% of 158 and 66% of 172 bulimic women they studied, respectively, reported victimization by physical or sexual assault, while Bulik et al. (3) reported that 34% of 35 bulimic women they studied acknowledged sexual abuse. Palmer et al. (4) assessed the memories of childhood sexual experiences with adults of 158 women with eating disorders, reporting that one-third of these women acknowledged childhood victimization through sexual abuse, and over one-half described some adverse sexual experience. Similarly, in research on sexually abused women, eating disorders and body image disturbances are often identified (5).

Our finding that 49% of 39 subjects spontaneously revealed histories of sexual abuse differs from previous reports, wherein such information was elicited from participants as a primary research focus. We can only speculate whether 49% may underrepresent the actual number of sexually abused bulimic participants, and how many more participants might have revealed histories of childhood sexual abuse if the question had been directly addressed.

While it has been recognized that sexual abuse is not uncommon, the prevalence of sexual abuse in both the general population and clinical populations has been difficult to determine conclusively. At this time it is unclear how much, if any, these occurrence rates differ from base rates of sexual abuse in the general population or in specific clinical populations. Additional research addressing the relation between childhood victimization through sexual abuse and later development of bulimia could be a valuable addition to literature concerning both bulimia and sexual abuse.

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Stolen Objects as Transitional Objects

SIR: The excellent review by Marcus J. Goldman, M.D. (1) on kleptomania cited the statement by Simpson and Porter (2) that this behavior may be driven by "more primitive behavior patterns originating in painful encounters with hostile caretakers during the first years of life." In line with this explanation, and borrowing from Winnicott's (3) notion of the "transitional object" as working because it is both *of* the mother and yet *not* the mother, I offer a vignette from the long analysis of a woman who was abused as a child and who, as an adult, suffered from many symptoms, including kleptomania. She reported in an analytic hour that she had seen my coat in the coat closet, had rubbed her cheek over the sleeve, and had had an intense desire to steal the coat. When I asked her what would happen if I gave her the coat, she told me that it would be useless to her; only if it still *belonged* to me could she steal it and thus have (something of) me.

Perhaps some simple, if partial, sense can be made of the nonsense of compulsively stealing objects by understanding them precisely as *stolen* and understanding that their value lies in their belonging to others. Thus, they can function as transitional objects, with the compulsion to steal them expressing the need to take (back?) a piece of the denying, abusing, or otherwise failed early caretaker.

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Gender Differences in Schizophrenia

SIR: Michael Flaum, M.D., and associates (1) reported that women suffering from schizophrenia, unlike their male counterparts, do not show statistically significant ventricle enlargement. We are concerned about this study because the authors used what we feel are unusual data (for female control subjects) in formulating the profound speculation that gender differences described in the clinical manifestations of schizophrenia may relate to fundamentally different underlying pathophysiologies.

The column heading "Evidence of Gender Difference in VBR [ventricle-brain ratio] Found in Study" in table 1 is misleading in the broader context of the article. This heading refers to differences between male and female schizophrenic patients rather than differences between ill and well within-gender groups. In fact, except for the authors' own studies, the reports cited do *not* show differences in the comparisons of female patients and control subjects versus male patients and control subjects. Further, a study of monozygotic twins discordant for schizophrenia

(2) found that in pairs of twins, the ill female twins had the larger ventricles just as did the ill males.

When Dr. Flaum and associates compared ill versus well within-gender subjects in the last three of their own studies listed in table 2, they found differences between males but not females. However, the VBR values for the female control subjects in those three studies were highly atypical, because they were greater than those for the male control subjects. To our knowledge, in over 40 years of studies involving post-mortem measurements of ventricle volume (3, 4) and CT scan studies of VBR in normal subjects (5), as well as in the normal subjects described in table 1 and elsewhere, it has been consistently demonstrated that mean ventricle size and VBR are larger in males than in females.

We feel that it is more likely that the gender effect claimed by Dr. Flaum and associates came from the control population rather than from the patients. To test our hypothesis, we reanalyzed the data from the authors' studies (i.e., CT-2, MRI-1, and MRI-2), using the female control subjects as the comparison group for the male schizophrenic subjects. Although comparisons between these groups should, if anything, accentuate differences, *none* of the comparisons showed a significant difference, suggesting that something was unusual about the female control subjects. Further, a comparison of VBRs for male and female patients showed no significant differences. When the female patients were compared with the male control subjects, there were strong trends for larger ventricles in the female patients (one-tailed *t* tests, $p < 0.03$, $p < 0.07$, and $p < 0.08$, respectively, for CT-2, MRI-1, and MRI-2). Therefore, we conclude even from these data that female schizophrenic subjects have ventricles that are about as enlarged as those of male schizophrenic patients.

Even if gender differences are noted in the clinical syndromes of schizophrenia, this may reflect a process other than differing underlying pathophysiologies. Certainly, there is more diagnostic psychopathology in common between male and female patients than not. We think it a long leap to suggest differing etiologies or even pathophysiologies on the basis of the current evidence. A less elaborate explanation might be that a similar insult, perhaps sustained early in development, is differently influenced later by other factors (e.g., hormonal, psychosocial), accounting for syndromic differences between males and females.

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SIR: Dr. Flaum and associates reviewed several controlled CT studies that examined gender differences in schizophrenia and concluded that ventricle enlargement in schizophrenia is a predominantly male effect. However, we believe that this conclusion is premature. In only one of the 14 reviewed studies was a statistically significant difference between males and females reported. Takahashi et al. (1), using a "global impression scale," reported that schizophrenic males have more "abnormality in the left lateral ventricle" than do female patients. In addition to the studies reviewed by Dr. Flaum and colleagues, six other CT studies that compared lateral ventricle findings in male and female schizophrenic subjects failed to detect a significant gender effect (reference list available on request).

In support of a gender difference, Dr. Flaum and associates noted that in three of their own studies, male patients had larger ventricles than male control subjects, but in only one did female patients have larger ventricles than female control subjects. This result was obtained because there was a trend among schizophrenic patients for males to have larger ventricles than females and among control subjects for females to have larger ventricles than males. The trend toward larger ventricles in male schizophrenic subjects than in female schizophrenic subjects has been reported previously (2, 3). However, the trend for female control subjects to have larger ventricles than male control subjects is not found in any other study in which VBR values have been reported (2, 3).

Another possible explanation for the trends noted by Dr. Flaum and associates concerns the adequacy of the VBR as an estimate of ventricle size. A ratio of ventricle area to brain area from a single CT slice is used to control variability in ventricle size that is due to head size. This allows comparisons across individuals within the same study. Other investigators (4) have noted that this ratio does not adequately control physical and demographic influences on brain morphology and can introduce bias. In addition, females tend to have smaller craniums and smaller ventricles than males. The measurement of small ventricles from CT film is less reliable than the measurement of large ventricles and can include up to 40% measurement error (5). In some studies, small ventricles are reported as too small to measure. The reduced reliability for measuring small ventricles will increase error variance. Because females tend to have smaller ventricles than males, this will differentially affect data on females and reduce the probability of obtaining group differences between females. The volumetric ratios used in the two MRI studies reported by Dr. Flaum and associates are likely to be more accurate at estimating ventricle size than are the VBRs from CT scans. However, even with these measures and relatively large sample sizes, no significant differences are found between males and females.

In assuming that a simple ratio between ventricle size and brain size will be an adequate control for the many influences on brain morphology, Dr. Flaum and associates are perhaps trusting too much in currently accepted methods of measurement. While we agree that well-established gender differences in schizophrenia research make these authors' hypothesis theoretically appealing, they have failed to substantiate the hypothesis that gender plays a role in CT and MRI findings.

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Dr. Flaum and Associates Reply

SIR: The primary concern raised by Dr. Zigun and colleagues and Dr. Smith and colleagues is that our findings of ventricle enlargement in schizophrenia as a predominantly male effect may be based more on atypical female control samples than on our ill subjects. They note that in prior neuropathological and neuroimaging studies, male control subjects have typically been found to have larger VBRs than female control subjects, whereas we found a nonsignificant trend in the opposite direction in two of our three control groups.

Unfortunately, the available data on gender differences in ventricle size in both normal and psychiatrically ill subjects remain quite limited and inconclusive. The majority of studies do not find significant gender differences in either control or psychiatrically ill subjects. However, when differences are observed (regardless of statistical significance), they have consistently been in the direction of males having a greater ventricle size than females in both control and ill samples. Thus, the concern that our control groups could have been atypical is valid, and one that we recognized and shared in our report.

When a very similar gender pattern was observed in two consecutive samples, however, we felt that it deserved further attention and investigation. Our first step was to ensure that the samples were entirely independent by eliminating any subject who participated in both studies. After doing so, we found that the observed gender effect was unchanged. We then carefully reviewed our sampling methods to see if we could determine why the gender pattern among our control subjects might have been atypical, but we could not identify a sampling bias. We did note, however, that in the one study in which we used "medical control subjects" (i.e., subjects selected from radiology files that had been read as normal), the gender pattern among control subjects was more consistent with the literature; that is, there was a trend for the male "control" subjects to have larger VBRs than the females. In the two samples in which healthy control subjects were recruited from the community, this pattern was not found. If, in fact, the actual distribution of VBR values is broader for females than males, then samples of "medical control subjects" may be artificially truncated.

It is, of course, possible that a sampling bias went undetected or that, by chance, we recruited two atypical samples. But as we had no reason to discount our findings, we felt an obligation to report them fully and to try to make sense of them in light of what is currently known about schizophrenia. We did stress that no simple Gender by Diagnosis interaction

was found and that we could not draw definitive conclusions from the available data. We then delineated reasons that a model in which males would be more vulnerable to a type of schizophrenia characterized by ventricle enlargement would be theoretically appealing. We see the model that we proposed as no more "elaborate" or "profound" than Dr. Zigun and associates' speculation that schizophrenia is ultimately explainable by a single pathological mechanism to which both sexes are equally vulnerable. It may be that the admitted tentativeness and speculative nature of our discussion was not appropriately reflected in the title of the report. In fact, when we initially submitted the manuscript, the title concluded with a question mark, but this was omitted in revisions.

We are gratified that our report has drawn attention to the issue of gender in morphological studies of schizophrenia, and we hope that future studies consistently include gender analyses so that this issue can be more fully explored.

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Schizophrenia: More Than Two Disease Processes?

SIR: Raquel E. Gur, M.D., Ph.D., and colleagues (1) presented an important finding that may have major implications for schizophrenia research. Their principal components analysis on items that are regarded as negative and positive symptoms yielded three factors, rather than the two that would be expected from the perspective of a negative-positive distinction. Attentional impairment, bizarre behavior, and thought disorder did not load highly on negative or positive symptom factors but emerged as a third and discrete factor. The authors remarked that this finding should be replicated to warrant further discussion. This finding is, in fact, a replication of findings in three earlier studies (2-4) and partly consonant with the findings from a recent study (5).

Lewine et al. (2) found that bizarre behavior and loosening of associations showed a poor fit to scales of positive and negative symptoms developed with Rasch models. Using principal components analysis, Bilder et al. (3) found three symptom factors: a negative symptom factor (affective blunting, anhedonia, and avolition-apathy), a positive symptom factor (hallucinations and delusions), and a third factor, which showed high loadings of attentional impairment, alogia, bizarre behavior, and thought disorder. This factor was significantly correlated with neuropsychological deficits that implicated early neurodevelopmental compromise. Liddle (4) also used principal components analysis and found three factors, the component items of which were almost identical to those of Bilder et al. The statistical independence of thought disorder and bizarre behavior from both positive and negative symptom factors was reported recently by Arndt et al. (5). Thus, there are now a number of studies suggesting that attentional impairment, bizarre behavior, and thought disorder fall outside the negative-positive dichotomy (1-5). Additionally, my colleagues and I examined the relations of negative symptoms to premorbid functioning and provided correlational evidence for the lack of homogeneity of broadly defined negative symptoms (6).

It has been proposed that it may be necessary to consider two dimensions of pathology to understand the schizophrenic disease process. Although to the orthodox this may sound heretical, the emergent evidence suggests that more than two dimensions of pathology may have to be considered to explain the manifestations of schizophrenia. As discussed elsewhere

(6), this does not necessarily imply that there are multiple etiologies or discrete subtypes of the schizophrenic syndrome.

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Sense of Smell and Obsessional Behavior

SIR: David Brody, M.D., and associates (1) reported on the potential usefulness of olfactory assessment as an indicator of early CNS involvement in HIV infection. Little is known about the relation of the sense of smell to behavioral characteristics. We have assessed the sense of smell in five highly obsessional subjects and five normal subjects. All were women between the ages of 26 and 45 years. Obsessiveness was rated by scores on the Maudsley test for obsessive behavior (2) and the Yale-Brown Obsessive Compulsive Scale (3, 4). Sense of smell was tested with the University of Pennsylvania Smell Identification Test (5). Scores were converted into age and sex percentiles.

The results indicated clear differences in smelling acuity in the two test groups. The average Maudsley score was 3.8 for the normal subjects and 14.4 for the obsessional group (out of a possible 30). The average Yale-Brown score was 5.0 for the normal subjects and 15.6 for the obsessional group (out of a possible 40). The average performance on the Smell Identification Test was at the 84th percentile level for the normal subjects and at only the 57th percentile level for the obsessional group. To our knowledge, this potential difference in the sense of smell in obsessional patients has not been reported before. Such findings may be relevant to consideration of reporting impaired olfactory ability in medical subjects.

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Dr. Brody and Dr. Serby Reply

SIR: Ms. Goldberg and associates' findings are consistent with observations that dysfunction of the prefrontal cortex, basal ganglia, and thalamus may underlie obsessive thought and behavior. Baxter (1) demonstrated bilaterally increased glucose metabolism in the orbital cortex and striatum in patients with obsessive-compulsive disorder. Modell et al. (2) hypothesized that failure of striatal regulation of "frontothalamic neuronal interchanges" underlies production of obsessive and compulsive symptoms. Dysfunction of the orbitofrontal cortex and anterior temporal lobe is associated with olfactory disturbances in primates and humans (3). Odor identification deficits are also found in patients with known pathology in these anatomical areas, including those with Alzheimer's disease and those with Parkinson's disease (4).

Taken together with the observations of patients with HIV dementia reported in our article, Ms. Goldberg and associates' letter demonstrates how olfactory assessment may help to identify and localize CNS dysfunction. However, a few words of caution are in order regarding the interpretation of their data. The results could have been contaminated by significant depression, medications, and/or ritualistic interference with performance on the University of Pennsylvania Smell Identification Test. Future studies should control for these possible confounding factors.

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Treatment of Water Intoxication Due to Diuretics

SIR: René J. Muller, Ph.D., and Helen D. Lann, M.D. (1) described the case of a schizophrenic patient suffering from water intoxication due to polydipsia and simultaneous treatment with hydrochlorothiazide. I agree with their warning that "polydipsia should be ruled out before thiazide diuretics are prescribed for patients with schizophrenia," but I want to

emphasize that this precaution applies also to patients with diagnoses other than schizophrenia, since polydipsia is not confined to schizophrenic patients alone (2). I recently saw a case of water intoxication in a polydipsic patient with a diagnosis of vascular dementia who was being treated with bemethazide, a thiazide-type diuretic.

A further aspect to be discussed is the treatment that Drs. Muller and Lann's patient received. Obviously, the administration of hypertonic saline that led to an increase of serum sodium from 108 to 135 meq/liter within 8 hours was successful and well tolerated by the patient. It seems worth mentioning, however, that with this kind of treatment, such a good outcome is not warranted. Serum sodium was elevated at a rate of 3.4 meq/liter per hour, for a total increase of 27 meq/liter within 8 hours. There is considerable evidence that too rapid correction of hyponatremia may lead to often-fatal central pontine myelinolysis (3, 4). In general, 2 meq/liter per hour is considered the maximum rate for correction of serum sodium (3, 5, 6), with a maximum total increase of 15 meq/liter within the first 24 hours (2). I stress this point because otherwise readers might be inclined to think that the most rapid treatment of hyponatremia is the best treatment, an assumption that might turn out to be life threatening for the patient.

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Hip Fractures in Elderly Patients Taking Benzodiazepines

SIR: I am most puzzled by the report of Robert P. Hart, Ph.D., and associates (1) on the effects of buspirone and alprazolam on normal elderly subjects. A recent article describing the use of benzodiazepines in elderly subjects (2) documented that there were more hip fractures in patients taking benzodiazepines than in those who were not. Also, since the clinical effect of buspirone takes 4 or more weeks to occur (3), it seems unsound to conclude that there are no adverse side effects with this drug after only a 14-day trial. I would appreciate an explanation of these apparent inconsistencies.

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GEORGE A. ROGERS, M.D.
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Dr. Colenda and Associates Reply

SIR: We appreciate Dr. Rogers's concern about the use of psychotropic medication in elderly patients, especially the use of benzodiazepines and the apparent risk of comorbidity, such as falls and fractures. Ray et al. (1) reported a 70% increase in risk of hip fractures in Canadian patients receiving long-half-life benzodiazepines, compared to patients not receiving psychotropic medication. In patients receiving short-half-life benzodiazepines (such as alprazolam), no increased risk of hip fracture was found. The authors did not feel that their results were confounded by such factors as dementia, impaired ambulation, or functional status. Their results highlight the current expert opinion that long-half-life benzodiazepines should not be prescribed for elderly patients.

Our purpose was to examine how two psychotropic medications, alprazolam and buspirone, affected psychomotor performance in healthy elderly subjects in the absence of psychiatric and physical illness. We knew that buspirone did not adversely affect psychomotor performance in middle-aged adults (2-4). We were curious to see whether alprazolam, a high-potency, short-half-life benzodiazepine, affected psychomotor performance in elderly subjects in a manner similar to that of long-half-life benzodiazepines. Our results showed that buspirone, prescribed at 5 mg t.i.d., did not affect psychomotor performance in elderly patients and that alprazolam, prescribed at 0.25 mg t.i.d., had a minimal effect on psychomotor performance. These findings might have been different if higher doses had been used, especially for alprazolam.

The second question, regarding conclusions made about the medication after only a 14-day trial, can be answered in the following manner. Dr. Rogers is correct that the clinical effect of buspirone may take 4 weeks, but we were interested in the medication's effect on cognitive and psychomotor performance once plasma steady state was achieved. Given the pharmacokinetics of buspirone in elderly patients (5), a 14-day clinical trial was more than sufficient to see how this medication influenced performance.

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Nifedipine: Bite-and-Swallow Administration

SIR: We appreciate the letter by Morton Fier, M.D. (1) highlighting nifedipine use in the treatment of monoamine oxidase inhibitor (MAOI)-induced hypertension. Because of the risk of hypertensive crisis secondary to noncompliance with prescribed tyramine-free diets and interactions with nonprescription sympathomimetic amine drugs, many psychiatrists refrain from prescribing MAOIs despite their demonstrated efficacy in both depressive and anxiety disorders. Equipping patients who take MAOIs with nifedipine is a welcome treatment modality for decreasing the morbidity of hypertensive crises. In response to Dr. Fier's letter, we are concerned about how nifedipine should be administered.

Dr. Fier alluded to studies (2, 3) which have suggested that sublingual or buccal absorption of nifedipine results in a rapid and safe method of treating hypertension. Clinically, reduction in blood pressure occurs; however, these studies have not addressed the actual site of drug absorption. In a pharmacokinetic study, van Harten et al. (4) demonstrated that nifedipine capsules when bitten and swallowed are absorbed more rapidly from the gastrointestinal tract. The peak median plasma concentration following gastric absorption was significantly higher (71 ng/ml, compared to 10 ng/ml following sublingual administration) and peaks were reached earlier with gastric absorption. For sublingual administration, subjects held the contents of a nifedipine capsule under the tongue and did not swallow for 20 minutes. The oral cavity was then rinsed, and the original dose was recovered at a median proportion of 90%. In an earlier study, McAllister (5) showed that the bite-and-swallow method provided a more rapid response than either swallowing the capsule whole or administering the dose sublingually. As others have suggested (6), the results of pharmacokinetic studies support the hypothesis that the immediate effects of nifedipine are primarily due to gastric and not sublingual absorption.

The use of MAOIs requires extensive patient and family counseling to ensure compliance, safety, and efficacy. Patients also equipped with nifedipine capsules need specific information; this includes the reasons for compliance with the tyramine-free diet as well as indications for use of nifedipine, proper administration technique, and the profile of adverse effects. In an MAOI-induced hypertensive crisis, it is suggested that the patient bite and swallow the capsule for rapid effects while seeking emergency medical care.

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Issues Regarding Short-Term Abstinence in Outpatient Cocaine Addicts

SIR: The article "Changes in Brain Glucose Metabolism in Cocaine Dependence and Withdrawal" by Nora D. Volkow, M.D., and associates (1), while offering new data regarding brain glucose metabolism in cocaine addicts, did not detail important information regarding the research subjects. The study subjects were 15 outpatients who were recovering cocaine addicts reported to be in short-term abstinence. How were subjects' reports of no cocaine or other substance use validated? This detail is particularly important in studies of outpatients, who have ready access to cocaine.

In the Discussion section, the authors suggested that the higher metabolic activity observed less than a week after alleged last cocaine use may represent a nonspecific expression of drug withdrawal. However, is it not plausible that this activity represented brain functioning after recent use of cocaine rather than an excitatory state secondary to abstinence? Our group (2) did not observe a secondary excitatory state, or "rebound hyperexcitability" (3), in cocaine addicts who were undergoing short-term cocaine abstinence in a residential setting. Addicted subjects in our study demonstrated highest levels of mood distress immediately after the last cocaine use and no signs of autonomic hyperexcitability during early abstinence.

I question whether there is an endogenous cocaine withdrawal syndrome in inpatients. Excitatory states noted in newly abstinent cocaine addicts undergoing treatment as outpatients (4) may be an expression of classical conditioning (exposure to environmental cues of persons, places, and objects associated with cocaine use [2]) rather than direct effects of sudden deprivation of cocaine from dopamine or other receptors in the brain, as suggested by Dr. Volkow and associates. It is important for future research to differentiate better how classically conditioned effects of drug use are mediated during active use and abstinence as compared to a substance's direct receptor effects.

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Dr. Volkow and Associates Reply

SIR: Dr. Weddington is correct in pointing to the uncertainties of ascertaining time of last cocaine use when studying outpatient cocaine abusers. Our strategy was documentation of each subject's drug history by two different investigators and a research nurse. Although the information obtained was cor-

cordant in the three reports, it is possible that the subjects may have consistently lied.

We do not see a cause for disagreement between the other points brought up by Dr. Weddington and our own data. Similar to his experience (1), our subjects did not have evidence of autonomic hyperarousal (we never stated that increased brain metabolism is equivalent to increased autonomic activity), and as can be seen in our table 1, both affective symptoms and cocaine craving were higher in subjects tested during the first week of detoxification.

We agree that cocaine withdrawal is distinct from the "classical" withdrawal reported for drugs such as alcohol and opiates and did not make any other implication. Our statement was that "the higher metabolic activity observed less than a week after cocaine withdrawal may represent a nonspecific expression of drug withdrawal." This statement is equivalent to "this activity represented brain functioning following recent use of cocaine." Whether to call it cessation, discontinuation, or drug withdrawal becomes a semantic issue. What is relevant is the understanding of the mechanisms underlying the response of the brain to cocaine discontinuation. We believe that this response is in part related to dopamine brain activity.

Could the findings reported in our investigation represent "an expression of classical conditioning (exposure to environmental cues of persons, places, and objects associated with cocaine use)"? Although it is highly unlikely that the positron emission tomography procedure in itself could serve as a trigger for cocaine-induced craving, the increased metabolic activity seen during the first days of cocaine cessation could relate to a functional pattern that accompanies the state of heightened sensitivity to cocaine-related external cues.

Unfortunately, we do not have enough knowledge to link particular patterns of brain metabolic activity with specific mental states. Nor can we assume that the expression of conditioning-induced cocaine craving is independent of neurotransmitter function.

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NORA D. VOLKOW, M.D.
ROBERT HITZEMANN, PH.D.
JOANNA S. FOWLER, PH.D.
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Upton, N.Y.

Risks of Restraints Versus Psychotropic Medication for Pregnant Patients

SIR: The letter from William H. Miller, M.D., and Michael P. Resnick, M.D. (1) on the use of restraints for violent pregnant patients called attention to an important issue and highlighted the difficulty in choosing between "interventions with complex and occasionally unknown risk-benefit ratios." However, some errors and omissions in their account prompt our response.

First, we question Dr. Miller and Dr. Resnick's conclusion that the use of restraint is a "lesser risk and a more easily reversible decision" than psychotropic medication. They asserted that "the impacts of medication on pregnancy, mother,

and fetus are well described." As psychiatrists who specialize in the treatment of pregnant patients, we only wish that were true! In fact, it is not established that agents used in the emergency treatment of violence—typically, neuroleptics and/or benzodiazepines—pose lasting adverse risks to the so-called "obviously pregnant" (by which we assume the authors meant second or third trimester) patient (2, 3). Especially, we do not know whether brief exposure to psychotropic medication in an emergency situation is of any significant consequence.

Regarding reversibility, although restraints themselves can readily be removed, their adverse psychological consequences may be long lasting. The authors' case report suggests that it was impossible to establish meaningful rapport and a therapeutic alliance with this patient, given the repeated court proceedings, violence against staff, and paranoid delusions about staff. Administering antipsychotic medication may, in such instances, be less traumatic and alleviate delusions sufficiently to build a working relationship, while restraints may intensify paranoia.

Of course, the absence of known adverse effects of fetal exposure to psychotropic drugs does not permit injudicious use of these drugs. However, one must also consider the risk of alternative treatments and the risk of withholding pharmacotherapy. The psychotic pregnant patient not uncommonly has beliefs and behaviors that may place her fetus in jeopardy (4). These include delusional refusal of prenatal care, psychotic denial of pregnancy, refusal of adequate nutrition, attempted premature self-delivery, precipitous delivery, fetal abuse, and neonaticide. The delusional basis of most of these high-risk behaviors is more likely to respond to pharmacotherapy and psychosocial measures than to restraint alone.

Despite the risks, we agree that in some cases restraints are necessary during pregnancy. For this reason, we would like to comment about the authors' recommendations for restraint technique. An important factual error is their suggestion to raise the patient's "left hip" with a pillow to avoid aortocaval obstruction by the gravid uterus. It is the *right* hip that should be raised for left uterine displacement (5). Also, restraint during pregnancy may pose extra discomforts; increased urinary frequency and pruritus are common accompaniments of pregnancy that could become unbearable if special provisions are not made for their alleviation.

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Dr. Miller and Dr. Resnick Reply

SIR: The complexities of psychiatric intervention with violent pregnant patients invite many diverse and emotional opinions. We appreciate the response to our letter and the oppor-

tunity to discuss further the significant concerns in caring for the often neglected, psychiatrically ill pregnant patient. We would like to emphasize three points.

We advocate *consideration* of restraints after failure of other noninvasive methods *and* when the etiology or duration of the behavior is not known, as in intoxication with a psychoactive substance or acting out in which psychotic symptoms are not found. Even under these circumstances, at times, psychopharmacologic intervention may be the most appropriate. We agree that patients with a psychotic presentation should be treated with medication when appropriate. Withholding any appropriate treatment is not good medicine or good psychiatric care.

In regard to the repercussions of various treatment modalities, the limited information *known* about the impact of medication on pregnancy is, indeed, well described (1, 2). Unfortunately the long- and short-term consequences of using psychotropic medication during any stage of pregnancy are not very clear and most likely will never be known. We agree that the impact of restraints on the patient and on the therapeutic relationship also needs careful consideration. No intervention should be made without looking at all its known risks and benefits. Clinicians need to be well informed and cautious but also open to all appropriate treatment options.

We appreciate the clarification regarding which hip should be elevated when restraining a pregnant patient. The most important aspect of care is to avoid having the patient horizontal and flat on her back. Positioning the patient on either side or in the inclined Fowler's position will improve vena caval flow. Frequent checks of the patient and rotation of her position are crucial in preventing problems such as frequent urination and pruritus.

One must consider all options when dealing with psychiatric presentations during pregnancy. The rights of both mother and fetus need careful consideration. The ethical and medical questions raised in the treatment of the psychiatrically ill pregnant patient need further discussion and research.

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Further Comments on Projective Identification

SIR: I wish to thank William N. Goldstein, M.D. (1) for bringing the subject of projective identification to the attention of *Journal* readers. I am impressed by Dr. Goldstein's integrative efforts but wish to call attention to what I believe is the fact that the concept of projective identification underwent a "sea change" (2) when it came over to America. The original Kleinian intrapsychic conflictual perspective became eclipsed by the newer interactional one. Because of the limitations of space, I wish to emphasize three aspects that differ from Dr. Goldstein's thesis.

First, the identification component of projective identification is, from the intrapsychic conflictual perspective, always experienced only by the projecting subject, not the object.

When the object (therapist) experiences the projection, that is termed the "therapist's projective counteridentification" or "introjective identification." Thus, the subject who uses projective identification as a defense seeks first to disidentify with an aspect of himself and then reidentify it in the object, hoping thereby either to become the object (and thus disown himself) or to lose bad parts of himself in the object (split off) in order to evacuate them and to control the object at a distance. Since the defense mechanism of projective identification is a fantasy and a not wholly successful one, the projecting subject always feels both an estrangement from the projected part and an identification with it—thus the feeling of being persecuted by it (persecutory anxiety). The split-off part is always believed to persecute one, because it is a part of one which is denied but with which one remains identified, according to Klein (3). This is not to gainsay the importance of the therapist's parallel but separate coidentification with the patient's projective identification, a notion which Malin and I proffered after Bion (4), followed by my own contribution (5) and then by Ogden's noteworthy elaborations (2) of the therapist's participation.

Second, as a consequence of the foregoing, it is inconceivable that there can be a differentiation between projection and projective identification. The subject is always tied to his projection because he is identified with it and persecuted by it as a consequence. It is this consideration that is pivotal in distinguishing between persecutors and enemies. Further, the contents of the mind are believed thereafter to consist of subsequent introjective identifications with these projective "amalgams"; i.e., we become what we believe we have transformed our objects into by our projective identifications.

A third point of difference is the idea that object representations can be projectively identified. They cannot; they are displaced. There is an important difference between the Kleinian concept of the internal object and the classical concept of the object representation. The former is inextricably bound with parts of the self that have been projectively identified with it, whereas the latter has been "cleared" by the withdrawal of projective identifications and stands separate from the self representation. However, one can project *into* an object representation and transform it into an internal object.

Finally, projective identification, in its nondefensive form, can be seen in altruism, empathy, communication, and exploration (similar to the way bats use "sonar").

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SIR: Dr. Goldstein is to be commended for writing a very clear and comprehensive article on projective identification. He also noted a theoretical issue concerning whether or not, and under what circumstances, ego boundaries are "blurred" in projective identification. It is to this issue that I would like to direct my comments.

One of the most useful metaphors for distinguishing between borderline and psychotic personality organization (1) is Bion's notion (2) of the container and the contained. Psychological boundary (the container) should not be theoretically confused with psychological content (the contained). In borderline personality organization, with its corollary defenses of projection and introjection, the ego boundary is maintained, but the origin and location of psychological content is confused: is the anger, for instance, within the patient or the other person? In psychotic personality organization, the ego boundary is lost, and there is no differentiation between the intrapsychic self and object representations or the interpersonal self and other. Similarly, the origin and location of psychological content are irrelevant because an undifferentiated state exists. Intrapsychically, there is *fusion* between self and object representations, rather than a *confusion* of location, which always implies the existence of a boundary.

Projective identification, therefore, could be either a borderline or a psychotic defense, depending on whether the patient is confused by the location of psychological content and subsequently attempts to control the object or the patient's ego boundaries are lost, the location of content is irrelevant, and the object is experienced and controlled (intrapsychically and interpersonally) as an aspect of the self.

As Dr. Goldstein theorized, the projection of self or object representation appears to mark intrapsychically the likelihood of a psychotic or a borderline projective identification, respectively. I think the term "blurring," however, should not be used, since it obfuscates an important theoretical distinction between psychological content and boundary (3, 4).

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Dr. Goldstein Replies

SIR: Regarding Dr. Grotstein's letter, I agree with the majority of his ideas. Dr. Grotstein is an expert on such items as the "sea change" and the Kleinian use of the term "projective identification." I am sure that readers will find his letter very informative.

However, I do take issue with his idea that there is no difference between projection and projective identification. As I elaborated in my article, a good case can be made for that differentiation. This is in accordance with Kernberg (1), Ogden (2), Hamilton (3), and many others. Ultimately, the distinction (or lack of distinction) between projection and projective identification depends on one's definitions of these terms.

In reference to Dr. Grotstein's idea that object representations cannot be projected but can only be displaced, this again seems to be a matter of definition. I have always distinguished projection from displacement, just as Dr. Grotstein does; yet, as I elaborated in my article, some theorists equate the term "displacement" with what they call the "projection of an object representation."

Regarding Dr. Meloy's letter, I think his ideas differentiating borderline from psychotic mechanisms, although somewhat different theoretically from mine, are nonetheless very interesting and useful. However, I believe he misunderstood my intent in suggesting that I link the projection of a self representation with a psychotic mechanism and the projection of an object representation with a borderline mechanism. In fact, I link the projection of a self representation with either a psychotic or a borderline mechanism and the projection of an object representation with either a neurotic or a normal mechanism.

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Race/Ethnicity of Psychiatrists of the Future

SIR: A recent article, "The Future of Psychiatry: Psychiatrists of the Future" (1), contained a glaring omission. While the title suggests an open discussion of those who will populate psychiatry in the coming decades, the article made no mention of race or ethnicity. In fact, despite its title, most of the article was an analysis of gender changes in the composition of the psychiatric profession. Even if the article had been retitled to reflect its content, for example, "The Future Role of Women in Psychiatry," the issue of race/ethnicity would still not disappear, since women also come in all shades and hues. Moreover, it is not an acceptable rationale for the omission of data on race/ethnicity to state that the survey instrument does not contain such information. Even our U.S. Census Bureau, as stodgy an organization as we have, has increasingly collected data not only by race/ethnicity but by subgroups within racial and ethnic groups.

It has now become widely accepted that minorities and women will be the dynamic portion of our nation's future work force. Hence, this kind of omission is simply unacceptable in the 1990s and should not have passed through peer review.

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Dr. De Titta Replies

SIR: The point made by Dr. Nickens about the lack of information on race/ethnicity is well taken. This is an area about which there is considerable interest and concern.

The APA census of residents contains extensive demographic information, including race/ethnicity. The data demonstrated

interesting patterns of change in several areas, e.g., increases in the number of psychiatric residents, gender distribution, race/ethnicity, and source of medical degree, among others. Since to explore all of these areas in depth would have been beyond the scope of a single paper, a decision was made to narrow the focus to the first two, where the greatest changes were observed. We also indicated (p. 854) that a later report would address other demographic and training characteristics. For example, our preliminary review suggested that there might be important changes to report with respect to the racial/ethnic composition of the resident population, as well as interesting trends in the shifting number of international medical graduates in psychiatry, particularly in the subsets of U.S.-born versus foreign-born international medical graduates.

We will continue to analyze the results of each year's resident census and to inform the field of changes and their implications.

MARTA DE TITTA, PH.D.
Washington, D.C.

Funding of Child Psychiatry Programs

SIR: I read with interest the recent article by Robert S. McKelvey, M.D., about the crisis in funding child psychiatry programs (1). Since I head a child psychiatry program in the same region as Dr. McKelvey and was a faculty member at Baylor College of Medicine (from 1983 to 1986), I can contribute some further perspectives.

I agree that funding for child psychiatry programs has been quite deficient, as described in the Project Future report (2) and the Institute of Medicine report (3). I do disagree with Dr. McKelvey's use of the Baylor program as an example of these problems. The circumstances faced by that program were unique because of its dependence on the pediatric hospital and department for most of its funding. As cited by many authors, including Fritz (4) and Ahsanuddin and Adams (5), relations between departments of psychiatry and pediatrics involving child psychiatry programs are usually tenuous. This makes children's hospitals and pediatric departments unstable funding sources, always subject to academic politics. This was recognized by many faculty members at Baylor before the funding from Texas Children's Hospital was reduced.

Due to the early development of our subspecialty at particular academic centers, especially at The Johns Hopkins University under Adolf Meyer and Leo Kanner, child psychiatry became a subspecialty of psychiatry rather than pediatrics. This should imply that departments of psychiatry have the ultimate responsibility for the health and viability of child psychiatry programs. For many years child psychiatry programs were treated as "step-children" and/or even revenue generators for the rest of the department. In the past 5 years, numerous efforts among the Society of Professors of Child Psychiatry, the Association of Chairmen of Departments of Psychiatry, and the Academy of Child and Adolescent Psychiatry have led to improved funding from psychiatry departments and the National Institute of Mental Health for child psychiatry training and research. This has led to the rapid growth of a number of child psychiatry programs across the country. However, other programs still lack strong departmental support, thus forcing them to rely on unstable funding sources.

Child psychiatry programs should seek funding from external sources. However, such funding must fit the missions of teaching and research inherent in academic centers.

My final caution is about one source listed by Dr. McKelvey, the proprietary for-profit facilities. After having made

two attempts at developing joint programs with such facilities I have concluded that the mission of these facilities, and their corporations, is not consonant with the mission of academic centers. This is primarily due to the conflict between their short-term profit motive orientation and the long-term planning and development needed for academic programs.

The ultimate solution to this problem, as indicated in the Institute of Medicine report (3), is to provide for child and adolescent psychiatry the solid academic funding base it deserves, from both public and private sources. It is not by coincidence that ours is the specialty of greatest shortage in the United States, while the need for our expertise and contributions grows annually, as witnessed by rising psychosocial morbidity and mortality in our youth.

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ANDRES J. PUMARIEGA, M.D.
Galveston, Tex

Dr. McKelvey Replies

SIR: I very much appreciate Dr. Pumariega's thoughtful and stimulating response to my commentary on the coming crisis in funding child and adolescent psychiatry training. His letter focuses on three problem areas: the often tenuous relationship between academic departments of pediatrics, their teaching hospitals, and child psychiatry; the lack of support by some departments of psychiatry to child psychiatry divisions; and the pitfalls of using for-profit hospitals as a funding source for child psychiatry training.

Dr. Pumariega's experience in our child psychiatry division came during the time it was based entirely at a tertiary-care pediatric teaching hospital. Although this situation may, in fact, have been unique, my impression from talking with other heads of child psychiatry divisions nationwide is that all of our programs are "unique." Each of us relies heavily on the support of some entity—a hospital, a medical school, a state government—that largely determines our fate. I would argue that Texas Children's Hospital was and is quite generous in its support of child psychiatry. Our need to seek an additional major training site for our program 4 years ago was dictated by rapid changes in the health care marketplace. The hospital administration worked closely with us to develop new alliances that would strengthen and broaden our basis of support. In many respects, our position is now an enviable one, spanning the full continuum of child and adolescent mental health services from pediatric consultation to an acute psychiatric hospital, residential treatment center, day hospital, and outpatient clinic (1). With careful management, and good fortune, we have the opportunity not only to pay our way but to earn excess revenues to use for training.

The relationship between psychiatry and child psychiatry within our department has been, during my experience here

a good one. We are expected to generate funding for our resident stipends and for most faculty positions through patient care revenues. This does not distinguish us, however, from other programs within the department, which is part of a private medical school.

I would certainly agree with Dr. Pumariega's comments concerning the pitfalls of dealing with for-profit hospitals. Our experiences with them have been varied; some good, others not so good. A number of our residents appreciate the opportunity to see a different style of delivering mental health care and have been complimentary about their specialized substance abuse and day treatment programs. On the other hand, we too have seen how the profit motive can interfere with our teaching objectives. Our approach has been to utilize the for-profit hospitals for training, but to do so with care, particularly in our choice of attending physicians with whom our residents work. For-profit hospitals are certainly a dominant feature on our health care landscape and one we cannot afford to bypass entirely.

Finally, I would certainly agree with Dr. Pumariega that child and adolescent psychiatry training deserves to be well supported, given the severe shortages in our ranks. The question is, of course, who will foot the bill? My article was an attempt to point toward the varied sources we will have to tap in order to sustain our training programs.

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ROBERT S. MCKELVEY, M.D.
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Greed as a Kleinian Term

SIR: In response to the letter of Paul L. Kingsley, M.D. (1) about the term "greed" and the lack of reference to it in the psychiatric literature, one can certainly find this term discussed in the teachings of Melanie Klein. Although I am currently in training and not qualified to summarize the contributions that Melanie Klein has made to the field of psychiatry, I have been introduced to her work and was moved to reply to Dr. Kingsley. In Hanna Segal's *Introduction to the Work of Melanie Klein* (2), greed is defined as "aiming at the possession of all goodness that can be extracted from the object, regardless of the consequences; this may result in the destruction of the object and the spoiling of its goodness, but the destruction is incidental to the ruthless acquirement." This is to be contrasted with envy, which is defined as "aiming at being as good as the object, but, when this is felt as impossible, it aims at spoiling the goodness of the object, to remove the source of envious feelings."

Other current sources in which summaries of Klein's discussion of greed and her psychodynamic theory of development can be found are *A Dictionary of Kleinian Thought* (3) and *Psychoanalytic Terms and Concepts* (4).

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"Cerebroversion" Instead of "ECT"

SIR: We have followed with great interest the discussion in the *Journal* regarding a new name for ECT (1-3). In general, we agree with Dr. Kellner and Dr. Ramsey (1, 3) that such a name change might be beneficial. During President Bush's recent difficulty with atrial fibrillation, the term "cardioversion" was used quite frequently and was explained by the news media in a way that was not frightening to the general public. This term was also mentioned in the original letter from Dr. Kellner and Dr. Ramsey (1). Therefore, we suggest the term "cerebroversion" as a more palatable substitute for "ECT." In explaining this option to patients, the analogy to cardiac dysrhythmias could be made, and depression (and other diseases responsive to cerebroversion) could be explained as a "cerebral dysrhythmia," which could be treated with either medication or cerebroversion.

We hope that other psychiatrists find this term, and the explanation of its effectiveness, useful in their practice.

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JEFFREY H. MORSE, M.D.
DELMAR D. SHORT, M.D.
EDWARD A. WORKMAN, M.D.
KATHLEEN LEWIS ELNAGGAR, M.D.
Salem, Va.

Dr. Kellner Replies

SIR: We appreciate the efforts of Dr. Morse and associates to continue the search for a new name for ECT. We feel that "cerebroversion" is close but not quite right. Our discomfort is with the fact that calling depression a cerebral dysrhythmia is really stretching things a bit too far. While ECT does indeed profoundly change EEG rhythms, there is little evidence that waking EEG rhythms are consistently "dysregulated" in depressive patients. Another practitioner has suggested the name "electroencephalotherapy" (EET) (1) because of its similarity to EEG, a neutral and well-accepted term. This, too, is not bad but still not charismatic enough.

Changing names is clearly a very difficult and painful proposition. If done correctly, however, it could be of great help to our patients and our profession. We remain hopeful that when the right name comes along we will know it. Madison Avenue, are you listening?

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CHARLES H. KELLNER, M.D.
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Debate on the Osheroﬀ Case: Postscript

SIR: Hippocrates on medical treatment: "Life is short; art is long; opportunity fugitive; experience delusive; judgement difficult. It is the duty of the physician not only to do that which immediately belongs to him but likewise to secure the cooperation of the sick" (1).

Osler on science in medicine: "The practice of medicine is an art based on science" (2, vol. II, p. 88).

Osler on the medical profession: "We . . . are . . . ever beset with the common and fatal facility of reaching conclusions from superficial observations and constantly misled with the ease with which our minds fall into the ruts of one or two experiences" (2, vol. II, p. 89).

Osler on the aims of the medical profession: "To make perfect . . . the art of observation, to call to aid the science of experimentation, to cultivate the reasoning faculty so as to be able to know the true from the false—these are our methods. To prevent disease, to relieve suffering and to heal the sick—this is our work . . . to track to their sources the causes of disease . . . these are our ambitions" (2, vol. I, p. 281).

Burke on the law in America: "[Its] study renders men . . . prompt in attack, ready in defense, . . . who augur misgovernment at a distance and snuff the approach of tyranny in every tainted breeze" (3).

I saw Dr. Osheroﬀ with the late Dr. Nathan Kline in July 1978. (Dr. Osheroﬀ has given permission to discuss his treatment in this connection, and I am sending a copy of this letter to him.) He was prescribed doxepin and responded so well to medication that lithium was added a month later because of racing thoughts and extravagant ideas. Unfortunately, the opportunity was lost because his full cooperation had not been secured; he did not return for follow-up, relapsed, and was admitted to Chestnut Lodge in January 1979. The treatment had failed but the medication had not.

Dr. Stone and Dr. Klerman in their debate (4, 5, and elsewhere) agree that they would have treated Dr. Osheroﬀ with both medication and psychotherapy. No wonder Dr. Osheroﬀ felt aggrieved at wasting 6 months, and no wonder the case was settled out of court.

The difficulties of the art of medical treatment noted by Hippocrates persist, although we now have more science upon which to base this art and enlighten our experience and help our judgment. If used properly, it can prevent us from reaching conclusions from superficial observations or being misled by one or two experiences and can help us track to their sources the causes of disease.

I believe that Chestnut Lodge did not base its art on science, but the debate shows that views differ. Underlying the debate is the question, Who decides how we practice medicine? Increasingly, inevitably, and appropriately, economics (represented by utilization reviewers, insurers, government regulators, and the patient's finances) joins the art and the science of medicine in this debate. We will all need to "augur misgovernment at a distance," but the law itself may have to be the final protection and source of redress for both doctors and patients to "snuff the approach of tyranny in every tainted breeze": to prevent domination of treatment by the zealots, the regulators, or the ignorant.

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NIGEL BARK, M.B., B.CHIF
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Koro: Classification and Case Reports

SIR: Koro is a belief or delusion of retraction of the penis into the abdomen. In an elegant review paper, Ruth L. Bernstein, M.D., and Albert C. Gaw, M.D. (1) suggested that koro should be classified under somatoform disorders and proposed criteria for this disorder for DSM-IV. In addition the proposed that koro should be designated as a culture-specific syndrome. I would like to comment on these issues.

1. Since 1952 there have been 26 cases of koro reported in non-Chinese and non-Indonesian patients, including two of my cases (2). It is clear that koro is not exclusively a culture bound syndrome. Therefore, it should not be specified in this way in DSM-IV.

2. In non-Chinese subjects the syndrome is incomplete and does not include use of mechanical means to prevent penile retraction and/or fear of death with penile retraction (2, 3). In these patients one sees a belief or delusion of retraction of the penis into the abdomen associated with severe anxiety (2). This was the case with my patients (2). It is to be noted that even in the case of a Chinese man reported by Dr. Bernstein and Dr. Gaw, attempts at mechanical means to prevent retraction and fear of death were not present. Thus, I do not understand why Dr. Bernstein and Dr. Gaw included these two symptoms in their proposed criteria for koro. It is very likely that these symptoms are only present within the context of the culture-bound syndrome. In Western culture one sees the belief or delusion of retraction in association with anxiety. These, then, should be the major criteria. One may include the other criteria for the culture-bound syndrome. However, fulfilling the belief criterion should probably be adequate for non-culture-bound koro.

3. Koro can be associated with other primary psychiatric disorders, and it may be the primary disorder itself (2). As a primary disorder, this belief or delusion could lead to a secondary psychiatric disorder, e.g., depression, anxiety. This is demonstrated by the authors' case; the patient became suicidal when he did not improve. It is therefore important to identify koro on axis I while at the same time being able to document on axis I other pathology that may be the result of the koro belief or delusion. Placing koro under somatoform disorder allows this flexibility.

4. In addition to number 3 just listed, there is another major reason why koro should be classified under somatoform disorders. It is possible that koro could be a form of monosymptomatic hypochondriasis and/or monosymptomatic hypochondriacal psychosis. Within this context it is not clear whether the belief in retraction is an overvalued idea (4) or a delusion. Recent reports indicate that some forms of monosymptomatic hypochondriasis and/or monosymptomatic hypochondriacal psychosis may preferentially respond to serotonin reuptake blockers (5). Such specific treatments have no

been attempted for koro. Placing koro under delusional disorders and/or looking at this disorder as a secondary problem could restrict this potentially therapeutic approach. Koro should therefore be placed under somatoform disorders.

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DAVID A. FISHBAIN, M.D.
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SIR: Koro is a psychiatric disorder that is usually described as a culture-specific syndrome in Asian cultures, manifested by acute anxiety associated with the fear of genital retraction and the belief that complete disappearance of the penis into the abdomen will result in death. Even though some cases have been reported in non-Asian subjects (1-3), it is often referred to as a culture-bound syndrome. In their recent article, Dr. Bernstein and Dr. Gaw reported a case of koro in a Cantonese patient in the United States and proposed diagnostic criteria and a classification of koro for *DSM-IV*. I would like to report a case of koro that occurred in a clearly non-Asian cultural setting and that stirred up diagnostic controversy.

Mr. A was a 38-year-old man, married and the father of two children. He was initially referred to our treatment center for evaluation of sexual dysfunction. He had previously consulted a sexologist and a urologist for investigation and treatment of premature ejaculation. He had no other psychiatric or medical history. He used alcohol and hashish occasionally in small quantities.

During evaluation Mr. A reported that the problem of premature ejaculation had been present for many years and that erectile difficulties had appeared in the past 2 years and were causing increasing tension in his marital life. He also reported that he recently noticed that his penis was shrinking and was penetrating into his abdomen. This preoccupation was causing him a great deal of anxiety, as he feared that it could lead to serious physical damage. There were no symptoms or signs of an affective disorder, delusions, or other psychotic symptoms, but he had engaged in exhibitionistic activities in the past. He had had no significant contact with Asian culture.

The koro-like syndrome was preceded by a long history of sexual dysfunction and insecurity, which was heightened by recent tensions in his married life as a consequence of his sexual performance. The anxiety generated in such a context could have fostered castration fears or, from a psychophysiological perspective, a "self-incrementing causal loop," as described by Simons (4), leading to the emergence of the koro syndrome. A diagnosis of delusional disorder, somatic type, was made, and Mr. A was referred for psychiatric treatment. He did not follow this recommendation and was lost to follow-up for 2 years. He eventually developed a major depressive

episode that led recently to a second consultation. There was no evidence at this point of persistent koro features. His depressive episode responded to desipramine, 300 mg/day.

Initially, Mr. A's symptoms best fitted the *DSM-III-R* criteria for delusional disorder, somatic type, and there was no evidence of any major affective disorder. Given the diagnostic criteria proposed by Dr. Bernstein and Dr. Gaw, the diagnosis would have been genital retraction disorder, not culture-specific. The occurrence of major depression later on raises the possibility that the initial consultation could have been due to an undiagnosed affective disorder. Nevertheless, this case illustrates that given the right setting and stimulus, koro can indeed occur in cultures other than Asian.

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JOSE LUIS FABIAN, M.D.
Montreal, Que., Canada

SIR: The article on koro by Dr. Bernstein and Dr. Gaw made interesting reading. We want to report our experiences with a patient who presented with koro-like symptoms.

Mr. A, a 20-year-old man, was referred from the outpatient surgery department of the hospital. He presented with intense anxiety and sadness resulting from shrinkage of his penis. Shrinkage occurred when he exercised and during the act of micturition. His penis would return to normal size 10-15 minutes after completion of the particular event. He also complained of generalized lack of interest, difficulty in going to sleep, and poor erection while masturbating. He had been masturbating for about 2 years. There were no psychotic features and no fear of death due to the symptoms. The symptoms were of acute onset and had been present for about 2 months. There were no immediate stressors.

Psychiatric assessment revealed anxiety, depressed affect, hopelessness, preoccupation with the fear of losing his masculinity, and guilt about masturbation. We made the diagnosis of depressive disorder, not otherwise specified, and treated the patient with dothiepin, supportive psychotherapy, and sexual counseling. Mr. A completely recovered from his symptoms after 2 months of therapy and has now been asymptomatic for the past 3 months.

Our patient presented with koro-like symptoms as an accompanying feature of depressive illness, and he responded to antidepressant medication. The complete picture of koro was lacking, as fears of death due to penile retraction and disappearance of the penis into the abdomen were absent. Usually, isolated cases of koro have been reported to display incomplete symptoms and occur as a part of a primary psychiatric disorder (1), which was also true in this case. Fear of complete disappearance of the penis and death due to koro are uncommon in isolated cases, as was also true in this case.

This patient experienced penile retraction while exercising or micturating, which indicates a probable physiological basis. In another case, Oyeboade et al. (2) demonstrated a relation between penile shrinkage and physiological changes in penile circumference. They explained this in terms of dysfunctional autonomic control of penile size. Simons (3) stated that many men experience the sensation of genital shrinkage, which can lead to anxiety, especially in stressful situations, which in turn can cause a reduction in blood to the extremities, leading to more shrinkage of the penis and further anxiety, and the patient presents with koro or koro-like symptoms. Koro-like symptoms have been found to be associated with drug withdrawal, epilepsy, brain tumors, and syphilis, which further favors a physiological basis for koro, with cultural factors acting as reinforcers.

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RAKESH K. CHADDA, M.D.
SABITA SHOME, M.D.
Delhi, India

Self-Decoration and Diagnosis

SIR: Alan H. Ali, M.D., presented an interesting, albeit dangerous, correlation in his letter to the Editor (1). Al-

though he found a correlation in his practice between multiple earlobe piercing and borderline personality disorder, it is important to note that the relationship is neither significant nor specific.

The practice of ear decorating is performed in other parts of the world (2). Cosmetic alterations in Western society can have multiple dynamic meanings. Grumet (3), in his review of the psychodynamic implications of tattoos, discussed the role in the formation of identity, belonging, antisocial behavior, and sexuality. He noted that tattoos are a form of nonverbal communication and afford an opportunity for "dermatological diagnosis." Tattoos, however, are not diagnosis-specific. Self-mutilation, without suicidal intent, occurs in a variety of psychiatric disorders (4).

The physical presentation of a patient and its meaning to the individual's self-image (5) are critical elements in clinical diagnosis but do not supplant the need for a broad and rigorous clinical analysis. By linking a diagnosis to a cosmetic characteristic, we as clinicians run the risk of, at best, premature diagnosis and, at worst, clinical stereotyping.

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Reprints of letters to the Editor are not available.

Annual Index

Following is the comprehensive index for volume 148 of the *Journal*, which covers all material in January 1991 through December 1991. The complete citation for each article in the author index is listed under the name of the first author. Coauthors are listed alphabetically with a cross-reference to the first author; cross-references containing multiple first author names separated by semicolons indicate multiple articles by the coauthor. Book reviews appear in the author index under the name of the reviewer and in the subject index under the heading Books Reviewed; the books reviewed are arranged alphabetically by the surname of the book's first author or editor. In addition to being indexed by author name, letters to the Editor regarding articles published in 1991 are indicated in parentheses after the citations for those articles.

Each entry in the subject index is identified by the surname of the first author only; commas between names of authors of letters to the Editor indicate multiple letters. Two-letter abbreviations are used for months. Entries other than Special Articles, Regular Articles, Commentaries, and Clinical and Research Reports are given the following designations: editorial (editorial), In Memoriam (in mem), book review (bk rev), letter to the Editor (letter), and Official Actions (off acts). Corrections are cited with the articles to which they refer and under the heading Corrections in the subject index.

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Psychiatric disorders in 36 families with Wolfram syndrome. Swift, Je 775-779

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Abnormal caloric requirements for weight maintenance in patients with anorexia and bulimia nervosa. Weltzin, De 1675-1682

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Genetic epidemiology of bulimia nervosa. Kendler, De 1627-1637

High nocturnal body temperature in premenstrual syndrome and late luteal phase dysphoric disorder. Severino, Oc 1329-1335

Long-term outcome of antidepressant treatment for bulimia nervosa. Walsh, Se 1206-1212

Menopause-related affective disorders: a justification for further study. Schmidt, Jy 844-852

Thyroid function and postpartum depression (letter). Stewart, reply of Claman, Je 816

HALDOL® Decanoate 100

(HALOPERIDOL) INJECTION 100mg/mL

HALDOL® Decanoate 50

(HALOPERIDOL) INJECTION 50mg/mL

For IM Injection Only

The following is a brief summary only. Before prescribing, see complete prescribing information in HALDOL and HALDOL Decanoate product labeling.

Contraindications: Since the pharmacologic and clinical actions of HALDOL Decanoate 50 and HALDOL Decanoate 100 are attributed to HALDOL haloperidol as the active medication, Contraindications, Warnings, and additional information are those of HALDOL, modified to reflect the prolonged action.

HALDOL is contraindicated in severe toxic central nervous system depression or comatose states from any cause and in individuals who are hypersensitive to this drug or have Parkinson's disease.

Warnings: *Tardive Dyskinesia:* Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown. Both the risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, antipsychotic drugs should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that 1) is known to respond to antipsychotic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient on antipsychotics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome. (For further information about the description of tardive dyskinesia and its clinical detection, please refer to ADVERSE REACTIONS.)

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure. The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology. The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported. Hyperpyrexia and heat stroke, not associated with the above symptom complex, have also been reported with HALDOL.

Usage in Pregnancy: (see PRECAUTIONS—Usage in Pregnancy) *Combined Use With Lithium:* (see PRECAUTIONS—Drug Interactions)

General: Bronchopneumonia, sometimes fatal, has followed use of antipsychotic drugs, including haloperidol. Prompt remedial therapy should be instituted if dehydration, hemoconcentration or reduced pulmonary ventilation occur, especially in the elderly. Decreased serum cholesterol and/or cutaneous and ocular changes have been reported with chemically-related drugs, although not with haloperidol. See PRECAUTIONS—Information for Patients for information on mental and/or physical abilities and on concomitant use with other substances.

Precautions: Administer cautiously to patients: (1) with severe cardiovascular disorders, due to the possibility of transient hypotension and/or precipitation of anginal pain (if a vasopressor is required, epinephrine should not be used since HALDOL may block its vasopressor activity and paradoxical further lowering of blood pressure may occur; metaraminol, phenylephrine or norepinephrine should be used); (2) receiving anticonvulsant medications, with a history of seizures, or with EEG abnormalities, because HALDOL may lower the convulsive threshold. If indicated, adequate anticonvulsant therapy should be concomitantly maintained; (3) with known allergies or a history of allergic reactions to drugs; (4) receiving anticoagulants, since an isolated instance of interference occurred with the effects of one anticoagulant (phenindione). Concomitant antiparkinsonian medication, if required, may have to be continued after HALDOL is discontinued because of different excretion rates; if both are discontinued simultaneously, extrapyramidal symptoms may occur. Intraocular pressure may increase when anticholinergic drugs, including antiparkinsonian drugs, are administered concomitantly with HALDOL. When HALDOL is used for mania in bipolar disorders, there may be a rapid mood swing to depression. Severe neurotoxicity may occur in patients with thyrotoxicosis receiving antipsychotic medication, including HALDOL.

The 1, 5, 10 mg HALDOL tablets contain FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals, especially in those who have aspirin hypersensitivity.

Information for Patients: Mental and/or physical abilities required for hazardous tasks or driving may be impaired. Alcohol should be avoided due to possible additive effects and hypotension.

Drug Interactions: Patients receiving lithium plus haloperidol should be monitored closely for early evidence of neurological toxicity and treatment discontinued promptly if such signs appear. As with other antipsychotic agents, it should be noted that HALDOL may be capable of potentiating CNS depressants such as anesthetics, opiates, and alcohol.

Carcinogenesis, Mutagenesis and Impairment of Fertility: No mutagenic potential of haloperidol decanoate was found in the Ames Salmonella microsomal activation assay.

Carcinogenicity studies using oral haloperidol were conducted in Wistar rats (dosed at up to 5 mg/kg daily for 24 months) and in Albino Swiss mice (dosed at up to 5 mg/kg daily for 18 months). In the rat study survival was less than optimal in all dose groups, reducing the number of rats at risk for developing tumors. However, although a relatively greater number of rats survived to the end of the study in high dose male and female groups, these animals did not have a greater incidence of tumors than control animals. Therefore, although not optimal, this study does suggest the absence of a haloperidol related increase in the incidence of neoplasia in rats at doses up to 20 times the usual daily human dose for chronic or resistant patients. In female mice at 5 and 20 times the highest initial daily dose for chronic or resistant patients, there was a statistically significant increase in mammary gland neoplasia and total tumor incidence; at 20 times the same daily dose there was a statistically significant increase in pituitary gland neoplasia. In male mice, no statistically significant differences in incidences of total tumors or specific tumor types were noted.

Antipsychotic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of antipsychotic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

Usage in Pregnancy: Pregnancy Category C. Safe use in pregnancy or in women likely to become pregnant has not been established; use only if benefit clearly justifies potential hazards to the fetus.

Nursing Mothers: Infants should not be nursed during drug treatment.

Pediatric Use: Controlled trials to establish the safety and effectiveness of intramuscular administration in children have not been conducted.

Adverse Reactions: Adverse reactions following the administration of HALDOL Decanoate 50 or HALDOL Decanoate 100 are those of HALDOL haloperidol. Since vast experience has accumulated with HALDOL, the adverse reactions are reported for that compound as well as for haloperidol decanoate. As with all injectable medications, local tissue reactions have been reported with haloperidol decanoate.

*CNS Effects: Extrapyramidal Reactions—*Neuromuscular (extrapyramidal) reactions have been reported frequently, often during the first few days of treatment. Generally they involved Parkinson-like symptoms which when first observed were usually mild to moderately severe and usually reversible. Other types of neuromuscular reactions (motor restlessness, dystonia, akathisia, hyperreflexia, opisthotonos, oculogyric crises) have been reported far less frequently, but were often more severe.

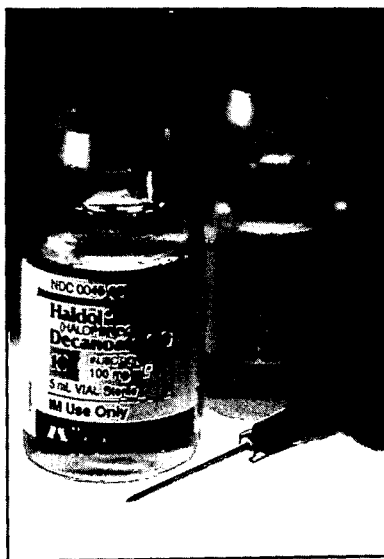
Severe extrapyramidal reactions have been reported at relatively low doses. Generally, extrapyramidal symptoms are dose-related since they occur at relatively high doses and disappear or become less severe when the dose is reduced. Antiparkinson drugs may be required. Persistent extrapyramidal reactions have been reported and the drug may have to be discontinued in such cases. *Withdrawal Emergent Neurological Signs—*Abrupt discontinuation of short-term antipsychotic therapy is generally uneventful. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain cases these are indistinguishable from "Tardive Dyskinesia" except for duration. It is unknown whether gradual withdrawal will reduce the occurrence of these signs, but until further evidence is available HALDOL should be gradually withdrawn. *Tardive Dyskinesia—*As with all antipsychotic agents HALDOL has been associated with persistent dyskinesias. Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients irreversible. The syndrome is characterized by rhythmic involuntary movements of tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities and the trunk. There is no known effective treatment for tardive dyskinesia; antiparkinson agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, this syndrome may be masked. It has been reported that fine vermicular movement of the tongue may be an early sign of tardive dyskinesia and if the medication is stopped at that time the full syndrome may not develop. *Tardive Dystonia—*Tardive dystonia, not associated with the above syndrome, has also been reported. Tardive dystonia is characterized by delayed onset of choreic dystonic movements, is often persistent, and has the potential of becoming irreversible. *Other CNS Effects—*Insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, and exacerbation of psychotic symptoms including hallucinations, and catatonic-like behavioral states which may be responsive to drug withdrawal and/or treatment with anticholinergic drugs.

Body as a Whole: Neuroleptic malignant syndrome (NMS), hyperpyrexia and heat stroke have been reported with HALDOL. (See WARNINGS for further information concerning NMS) *Cardiovascular Effects:* Tachycardia, hypotension, hypertension and ECG changes. *Hematologic Effects:* Reports of mild, usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tender toward lymphomonocytosis; agranulocytosis rarely reported and only in association with other medication. *Liver Effects:* Impaired liver function and/or jaundice. *Dermatologic Reactions:* Maculopapular and acneiform reactions, isolated cases of photosensitivity, loss of hair. *Endocrine Disorders:* Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia, hypoglycemia and hyponatremia. *Gastrointestinal Effects:* Anorexia, constipation, diarrhea, urinary retention, diaphoresis, a nausea and vomiting. *Autonomic Reactions:* Dry mouth, blurred vision, urinary retention, dyspepsia, priapism. *Respiratory Effects:* Laryngospasm, bronchospasm and increased depth of respiration. *Senses:* Cataracts, retinopathy and visual disturbances. *Other:* Cases of sudden and unexpected death have been reported in association with the administration of HALDOL. The nature of the evidence makes it impossible to determine definitively what role, if any, HALDOL played in the outcome of the reported cases. The possibility that HALDOL caused death cannot, of course, be excluded, but it is to be kept in mind that sudden and unexpected death may occur in psychotic patients when they go untreated or when they are treated with other antipsychotic drugs.

IMPORTANT: Full directions for use should be read before HALDOL or HALDOL Decanoate products administered or prescribed. For information on symptoms and treatment of overdose, see full prescribing information. The short-acting HALDOL injectable form is intended only for acutely agitated psychotic patients with moderately severe to very severe symptoms.

McNeil Pharmaceutical, McNEIL AB, INC., Spring House, PA 19477

8/23



In chronic schizophrenia...

A successful strategy for reducing relapse

74% reduction in relapse rates with haloperidol decanoate¹

- △ Helps reduce the number of hospitalizations
- △ Less volume per injection may enhance patient acceptance—an important factor in sustained protection from relapse
- △ Convenient, once-a-month dosing
- △ Less need for anticholinergics—a proven decrease in the number of patients requiring anticholinergics, over time¹

During dose adjustment or episodes of exacerbation of psychotic symptoms, therapy with HALDOL® Decanoate 100 or HALDOL Decanoate 50 can also be supplemented with short-acting forms of HALDOL (haloperidol). The scheduled use of the decanoate products are those of HALDOL. The prolonged action of HALDOL Decanoate 100 and HALDOL Decanoate 50 should be considered in the management of side effects.

Please see brief summary of Prescribing Information on adjacent page.

Start depot
therapy
with

HALDOL® Decanoate 100

(HALOPERIDOL)

INJECTION

100 mg/mL

HALDOL® Decanoate 100

(HALOPERIDOL) INJECTION 100mg/mL

HALDOL® Decanoate 50

(HALOPERIDOL) INJECTION 50mg/mL

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Drug Interactions: Patients receiving lithium plus haloperidol should be monitored closely for early evidence of neurological toxicity and treatment discontinued promptly if such signs appear. As with other antipsychotic agents, it should be noted that HALDOL may be capable of potentiating CNS depressants such as anesthetics, opiates, and alcohol.

Carcinogenesis, Mutagenesis and Impairment of Fertility: No mutagenic potential of haloperidol decanoate was found in the Ames Salmonella microsomal activation assay.

Carcinogenicity studies using oral haloperidol were conducted in Wistar rats (dosed at up to 5 mg/kg/day for 24 months) and in Albino Swiss mice (dosed at up to 5 mg/kg daily for 18 months). In the rat study survival was less than optimal in all dose groups, reducing the number of rats at risk for developing tumors. However, although a relatively greater number of rats survived to the end of the study in high dose male and female groups, these animals did not have a greater incidence of tumors than control animals. Therefore, although not optimal, this study does suggest the absence of a haloperidol related increase in the incidence of neoplasia in rats at doses up to 20 times the usual daily human dose for chronic or resistant patients. In female mice at 5 and 20 times the highest initial daily dose for chronic or resistant patients, there was a statistically significant increase in mammary gland neoplasia and total tumor incidence; at 20 times the same daily dose there was a statistically significant increase in pituitary gland neoplasia. In male mice, no statistically significant differences in incidences of total tumors or specific tumor types were noted.

Antipsychotic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of antipsychotic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

Usage in Pregnancy: Pregnancy Category C. Safe use in pregnancy or in women likely to become pregnant has not been established; use only if benefit clearly justifies potential hazards to the fetus.

Nursing Mothers: Infants should not be nursed during potential drug treatment.

Pediatric Use: Controlled trials to establish the safety and effectiveness of intramuscular administration in children have not been conducted.

Adverse Reactions: Adverse reactions following the administration of HALDOL Decanoate 50 or HALDOL Decanoate 100 are those of HALDOL haloperidol. Since vast experience has accumulated with HALDOL, the adverse reactions are reported for that compound as well as for haloperidol decanoate. As with all injectable medications, local tissue reactions have been reported with haloperidol decanoate.

CNS Effects: Extrapyramidal Reactions—Neuromuscular (extrapyramidal) reactions have been reported frequently, often during the first few days of treatment. Generally they involved Parkinson-like symptoms which when first observed were usually mild to moderately severe and usually reversible. Other types of neuromuscular reactions (motor restlessness, dystonia, akathisia, hyperreflexia, opisthotonos, oculogyric crises) have been reported far less frequently, but were often more severe. Severe extrapyramidal reactions have been reported at relatively low doses. Generally, extrapyramidal symptoms are dose-related since they occur at relatively high doses and disappear or become less severe when the dose is reduced. Antiparkinson drugs may be required. Persistent extrapyramidal reactions have been reported and the drug may have to be discontinued in such cases. **Withdrawal Emergent Neurological Signs—**Abrupt discontinuation of short-term antipsychotic therapy is generally uneventful. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain cases these are indistinguishable from "Tardive Dyskinesia" except for duration. It is unknown whether gradual withdrawal will reduce the occurrence of these signs, but until further evidence is available HALDOL should be gradually withdrawn. **Tardive Dyskinesia—**As with all antipsychotic agents HALDOL has been associated with persistent dyskinesias. Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients irreversible. The syndrome is characterized by rhythmic involuntary movements of tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities and the trunk. There is no known effective treatment for tardive dyskinesia; antiparkinson agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, this syndrome may be masked. It has been reported that fine vermicular movement of the tongue may be an early sign of tardive dyskinesia and if the medication is stopped at that time the full syndrome may not develop. **Tardive Dystonia—**Tardive dystonia, not associated with the above syndrome, has also been reported. Tardive dystonia is characterized by delayed onset of choreic or dystonic movements, is of ten persistent, and has the potential of becoming irreversible. **Other CNS Effects—**Insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo,

grand mal seizures, and exacerbation of psychotic symptoms including hallucinations, and catatonic-like behavioral states which may be responsive to drug withdrawal and/or treatment with anticholinergic drugs.

Body as a Whole: Neuroleptic malignant syndrome (NMS), hyperpyrexia and heat stroke have been reported with HALDOL. (See WARNINGS for further information concerning NMS.) **Cardiovascular Effects:** Tachycardia, hypotension, hypertension and ECG changes. **Hematologic Effects:** Reports of mild, usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tendency toward lymphomonocytosis; agranulocytosis rarely reported and only in association with other medication. **Liver Effects:** Impaired liver function and/or jaundice. **Dermatologic Reactions:** Maculopapular and acneiform reactions, isolated cases of photosensitivity, loss of hair. **Endocrine Disorders:** Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia, hypoglycemia and hyponatremia. **Gastrointestinal Effects:** Anorexia, constipation, diarrhea, hypersalivation, dyspepsia, nausea and vomiting. **Autonomic Reactions:** Dry mouth, blurred vision, urinary retention, diaphoresis, and priapism. **Respiratory Effects:** Laryngospasm, bronchospasm and increased depth of respiration. **Special Senses:** Cataracts, retinopathy and visual disturbances. **Other:** Cases of sudden and unexpected death have been reported in association with the administration of HALDOL. The nature of the evidence makes it impossible to determine definitively what role, if any, HALDOL played in the outcome of the reported cases. The possibility that HALDOL caused death cannot, of course, be excluded, but it is to be kept in mind that sudden and unexpected death may occur in psychotic patients when they go untreated or when they are treated with other antipsychotic drugs.

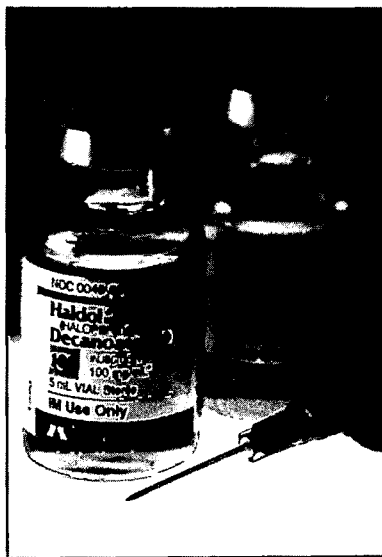
IMPORTANT: Full directions for use should be read before HALDOL or HALDOL Decanoate products are administered or prescribed.

For information on symptoms and treatment of overdosage, see full prescribing information.

The short-acting HALDOL injectable form is intended only for acutely agitated psychotic patients with moderately severe to very severe symptoms.

McNeil Pharmaceutical, McNEILAB, INC., Spring House, PA 19477

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In chronic schizophrenia...

A successful strategy for reducing relapse

74% reduction in relapse rates with haloperidol decanoate¹

- ▲ Helps reduce the number of hospitalizations
- ▲ Less volume per injection may enhance patient acceptance—an important factor in sustained protection from relapse
- ▲ Convenient, once-a-month dosing
- ▲ Less need for anticholinergics—a proven decrease in the number of patients requiring anticholinergics, over time¹

During dose adjustment or episodes of exacerbation of psychotic symptoms, therapy with HALDOL Decanoate 100 or HALDOL Decanoate 50 can be supplemented with short-acting forms of HALDOL or haloperidol. The side effects of the decanoate products are those of HALDOL. The prolonged action of HALDOL Decanoate 100 and HALDOL Decanoate 50 should be considered in the management of side effects. Please see brief summary of Prescribing Information on adjacent page.

Start depot
therapy
with

HALDOL[®] Decanoate 100

(HALOPERIDOL)

INJECTION

100mg/mL

Reference:
1. Youssef HA. A five-year follow-up study of chronic schizophrenics and other psychotics treated in the community. Depot haloperidol decanoate versus other neuroleptics. *Advances in Therapy*. 1989;4(4):186-193.

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